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"TO STUDY RELATIONSHIP OF HYPERTENSION WITH INSULIN RESISTANCE"

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INTRODUCTION

Hypertension (HTN) is one of the most significant and escalating global health issues. Hypertension is a changeable risk factor for cardiovascular disease, chronic renal failure, stroke, and a high incidence of mortality (GBD 2017)[1].

More than 1 billion people worldwide suffer from cardiovascular problems. They account for more than 10 million unnecessary deaths worldwide every year (Benjamin et al, 2017)[2]. There is a linear relationship between cardiovascular and cerebrovascular events and a broad range of blood pressure rise severity in clinical presentation. Each 20-mm Hg increase in systolic blood pressure or 10-mm Hg rise in diastolic blood pressure doubles the risk of cardiovascular and cerebrovascular events in people aged 40 to 70 (Rodgers et al., 2002; Gaciong et al, 2013)[3,4].

It is anticipated that the prevalence of hypertension would increase to > 1.5 billion by 2025 worldwide. More than fifty percent of people with diabetes mellitus (DM) have hypertension, which strongly contributes to both microvascular and macro vascular illness in diabetic patients (Lastra et al, 2014)[5]. Type 2 diabetes and hypertension are typical consequences. Compared to those with normal blood pressure (BP), those with hypertension are more likely to acquire diabetes. Previous prospective cohort studies have demonstrated that hypertension is an independent predictor of newly diagnosed diabetes (Tsiachriset al, 2011)[6]. About half of diabetic individuals also have high blood pressure, and those with hypertension have four times the risk of cardiovascular disease as those with normal BP. (Lastra et al, 2014)[5].

Theoretically, these pathways could remain over time, hence accelerating the progression of insulin resistance in hypertensive individuals. In addition, a recent study revealed that a faster advancement of insulin resistance is connected with an increased risk of incident diabetes (Wu et al, 2020)[7]. Obesity, oxidative stress, inflammation, and insulin resistance are regarded as common hypertension and diabetes pathways (Cheung and Li, 2012)[8]. Insulin resistance is common in people with high blood pressure, and both high blood pressure and insulin resistance are predictors of newly diagnosed diabetes mellitus (Petrie et al, 2018)[9]. But no research has looked at what a new diabetes diagnosis means for a person with both high blood pressure and insulin resistance. Insulin resistance and high blood pressure may cause a cycle that makes it easier for people to get diabetes.

Similar to the incidence of type 2 diabetes mellitus and it is estimated that hypertension is a significant public health issue in this region. Hyperinsulinemia and insulin resistance are frequent manifestations of hypertension (Naruse et al, 2019)[10]. Approximately half of people with essential hypertension are believed to be insulin-resistant. Insulin resistance is described as a reduction in the physiological response to insulin and a compensatory increase in insulin production. In this condition, glucose transport into skeletal muscle and fat cells is impeded. Therefore, hyperinsulinemia and hyperglycaemia are direct outcomes (Czech, 2017)[11].

Hyperinsulinemia may induce atherosclerosis directly by increasing LDL-cholesterol accumulation in artery walls, vascular smooth muscle migration, proliferation, amplifying connective tissue synthesis in the arterial wall, and slowing the regression of lipid plaques (Sowers, 1992)[12]. Several studies suggest a connection between essential hypertension and insulin resistance; however, the underlying pathophysiology appears intrinsically conflicting. It is crucial that further studies be proposed to examine the relationship between hypertension and other underlying diseases (Petrie et al, 2018)[13].

Due to demographic shift and westernization of lifestyle, the prevalence of obesity and its accompanying consequences has increased in Middle Eastern nations (Benjamin et al, 2017)[14].

According to recent epidemiological and pathophysiological studies, insulin resistance (IR) may be a significant primary cause of cardiovascular diseases (CVD). The effect of IR on the pathogenesis of hypertension has also been investigated extensively. The hyperinsulinemic-euglycemic clamp (HEC) is the current reference standard for assessing the importance of IR (Ormazabal et al, 2018)[15].Hypertension and insulin resistance is metabolic syndrome elements that commonly combine. According to clinical trials, up to 80% of people with type 2 diabetes also have hypertension, whereas around 50% of hypertensive people also have hyperinsulinemia or glucose intolerance (Zhou et al, 2012)[16]. By encouraging the production of nitric oxide (NO) in the endothelium and controlling salt homeostasis by enhancing sodium reabsorption in the kidney, insulin helps to control blood pressure. Recent studies have demonstrated that insulin resistance can develop in cardiovascular tissues as well as the more conventional insulin-responsive tissues, where insulin plays a role in the development of cardiovascular diseases including hypertension (Manhianiet al, 2011; Horita et al, 2011)[17,18].

Need for study- Insulin resistance has acquired a negative reputation and is viewed as harmful: it is usually connected with metabolic syndrome and hypertension, which raise the risk for type2 diabetes and cardiovascular disease. However, during the course of human evolution, insulin resistance may have been a necessary component of normal homeostasis to permit the redirection of nutrients to vital organs and a physiological adaptation to promote our ancestors' survival in times of starvation, infection, trauma, and stress. The same process may be chronically triggered incorrectly in the current era, causing hypertension, insulin resistance, or metabolic syndrome to develop. The purpose of the present study was to investigate the link between hypertension and insulin resistance.

Research hypothesis-This study will establish the insulin resistance in different grades of hypertension and will also help us to compare insulin resistance in healthy individuals and risk for developing hypertension.

AIM AND OBJECTIVES

AIM

To Study Relationship Of Hypertension With Insulin Resistance

OBJECTIVES

1. To estimate the insulin resistance in study population.

2. To co-relate insulin resistance with various grades of hypertension (Grade I, II)

Secondary objective:-

1. To estimate the insulin resistance in hypertensive and non-hypertensive patients.

REVIEW OF LITERATURE

High blood pressure is a risk factor for type2 diabetes and increases insulin resistance development (Petrie et al, 2018)[13]. Hypertension and insulin resistance are closely associated with an increased risk of impaired glucose tolerance, diabetes, cardiovascular diseases (CVD), and endocrine disorders.

In 2018, the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) issued a guideline for hypertension (Bakris et al, 2019)[19]. It is suggested that persons whose blood pressure is greater than 140/90 mmHg or who are using hypertension drugs be classified as having hypertension. Again, pre-hypertension was established if the blood pressure of patients without hypertension medication was 120–139/80–89 mmHg (Williams et al, 2018)[20].

Hypertension is a diabetes risk factor that can cause diabetes. Diabetes mellitus is defined by the American Diabetes Association (ADA) as fasting plasma glucose 126 mg/dL, oral glucose tolerance test (OGTT) 2 h plasma glucose 200 mg/dL, and HbA1C 6.5%, or by the use of antidiabetic drugs (American Diabetes Association Addendum, 2020)[21].

Recent research indicates that rapid evolution of insulin resistance may be connected with an elevated diabetes risk. Furthermore, it has been claimed that insulin resistance is the fundamental factor connecting hypertension and diabetes. These pathways could theoretically remain over time and accelerate the progression of insulin resistance in hypertensive patients (Lin et al, 2022)[22].

Hypertension

Among the flurry of recent guidelines for the management of cardiovascular disease (CVD), those for the treatment of hypertension are possibly the ones that have caused the most controversy. The series of studies that were compiled by the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, which came out of the National Heart, Lung, and Blood Institute, have served as the definitive guideline for the management of this disease. Since their introduction in 1976, these documents have played a prominent role in establishing standards for the treatment of hypertension. Other professional associations, such as the American Heart Association and the American College of Cardiology, have also made significant contributions to the treatment of hypertension. The

long-awaited eighth report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) on the management of hypertension ended a 9-year gap since the publication of the committee's seventh report (JNC 7). JNC 8 was also associated with a "minority report" that deviated in certain ways from the official guideline. Several challenging research published after the release of the new guidelines have further upset this subject (Wright et al, 2014)[23].

JNC 8 classification

- The primary hypertensive patients will be subjected to evaluation of hypertension grades as per JNC-8 classification Guidelines as shown in the table no.1

Table no.1

Hypertension	**Systolic blood pressure (mm Hg)**	**Diastolic blood pressure (mm Hg)**
Normal	<120	<80
Pre-Hypertension	120-139	80-89
Stage 1 Hypertension	140-159	90-99
Stage 2 Hypertension	≥160	≥100

Epidemiology

In pre-industrial societies, BP levels had narrow distributions with mean values that changed little with age and averaged around 115/75 mmHg, a value that probably represents the normal (or ideal) BP for humans. However, in most contemporary societies, systolic BP levels rise steadily and continuously with age in both men and women. This ubiquitous finding could be explained because age is a proxy for the probability and duration of exposure to the numerous environmental factors that increase BP gradually over time, such as excessive sodium consumption, insufficient intake of dietary potassium, overweight and obesity, alcohol intake and physical inactivity. Other factors, such as genetic predisposition or adverse intrauterine environment (such as gestational hypertension or pre-eclampsia), have small but definite associations with high BP levels in adulthood (Poulter et al, 2015)[24]. Even

modest rises in mean population BP lead to large increases in the absolute number of people with hypertension (Rose and Day, 1990)[25].

As economic development progresses, hypertension initially affects those with a high socioeconomic status, but at later stages of economic development, the prevalence of hypertension and its consequences are greatest in those with lower socioeconomic status; this phenomenon is seen both within and between countries. Further, the speed of change prevalence of hypertension since 2000 to 2010 has been much more rapid than in previous epidemiological transitions (Mills et al, 2016)[26].

Urban people are more at risk of these diseases as compared to their rural counterparts. As per the findings of National Family Health Survey (NFHS-4), the prevalence of hypertension, obesity, and blood glucose in urban area of Uttar Pradesh was 10.5%, 23.9, and 9.9%, respectively. However, the prevalence of the same phenomenon was 8.3%, 10.8%, and 8.2%, respectively in rural area (International Institute for Population Sciences, 2015-16)[27].

The estimates in the United States have demonstrated changes in crude estimates of the prevalence of hypertension from 31.9% to 45.6% based on 2017 ACC/AHA when compared with the JNC, and the proportion of individuals with hypertension who require antihypertensive therapy has increased from 34.3% to 36.2% (Muntner et al, 2018)[28].

Although global prevalence of hypertension is projected to increase based on the new criteria for classifying hypertension, the extent to which this impact on prevalence estimates in many countries including India, has not been evaluated. While prevalence of hypertension in India is estimated to range from 20% to 30% (Anchala et al, 2014; Bhise andPatra, 2018)[29,30], these estimates were based on the prior definition of hypertension according to the JNC7 guideline (Chobanian et al, 2003)[31].

Along with the global perspectives and reflections of the potential impact of the new guideline on the prevalence and management of hypertension in India (Wander and Ram, 2018)[32], a quantitative estimate of the prevalence and determinants of hypertension in India based on the new (2017 ACC/AHA) definition of hypertension is warranted. The new estimate will help guide the initiation, expansion, and implementation of intervention strategies for the prevention and management of hypertension in India.

Disease burden

Globally, 3.5 billion adults now have non-optimal systolic BP levels (that is, >110–115 mmHg) and 874 million adults have systolic BP ≥140 mmHg. Thus, approximately one in four adults has hypertension. Between 1990 and 2015 there was a 43% increase in the total global number of healthy life years lost to non-optimal BP, driven by population increase, population aging and a 10% increase in the age-standardized prevalence of hypertension(Forouzanfar et al, 2017)[33].

The Global Burden of Disease study has shown that non-optimal BP continues to be the biggest single risk factor contributing to the global burden of disease and to global all-cause mortality, leading to 9.4 million deaths and 212 million lost healthy life years (8.5% of the global total) each year (Forouzanfar et al, 2016)[34].

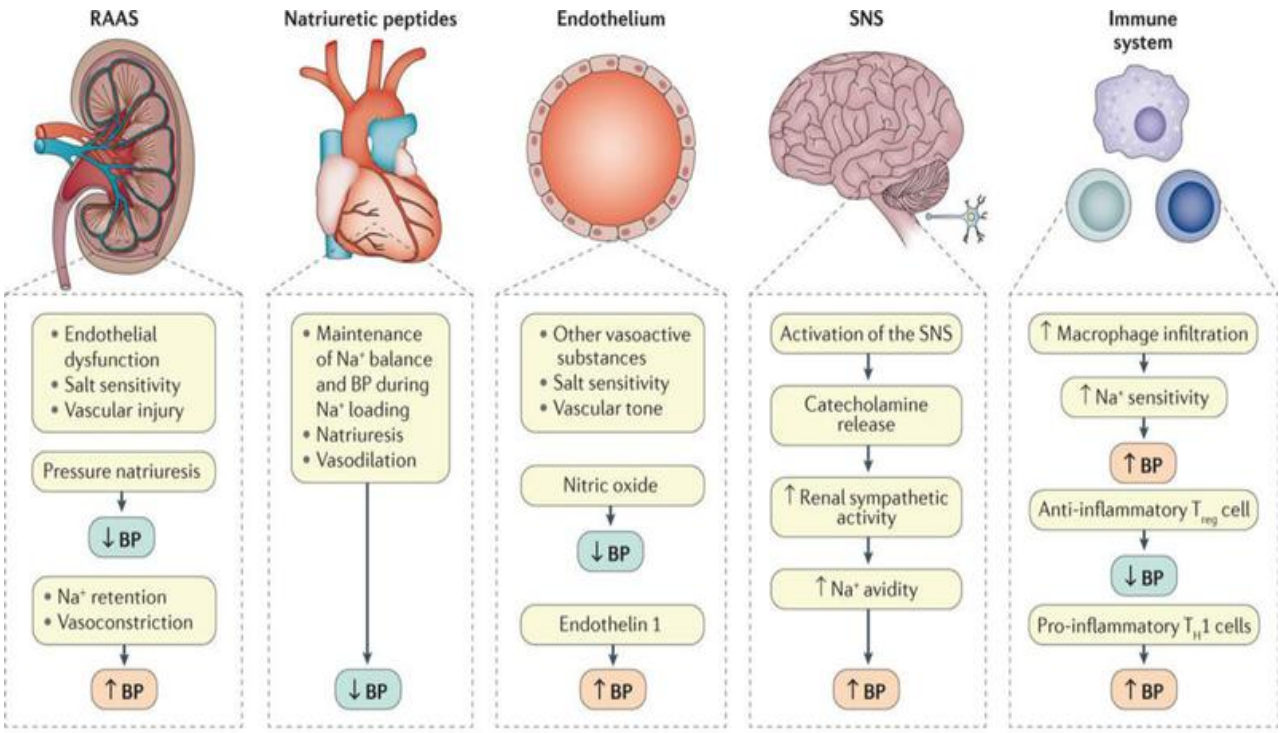
CVD risk

Prospective observational studies have repeatedly demonstrated a strong, continuous positive relationship between BP and CVD, with no evidence of a threshold for risk throughout the usual range of BP observed in clinical practice (Rapsomaniki et al, 2014)[35].

The relationship between BP and CVD applies to both systolic BP and diastolic BP, but is somewhat more robust for systolic BP in adults. It is noted in both sexes, at all ages throughout adulthood and for all major manifestations of CVD, including stroke (ischemic and hemorrhagic), coronary artery disease, heart failure, peripheral vascular disease and end stage renal disease (although there are variations in the strength of the associations and the slopes of the curves) (Rapsomaniki et al, 2014)[35].

The relationship is independent of other CVD risk factors, and level of BP has proven to be a major component of CVD risk in all prediction models (Goff et al, 2014)[36].

Approximately two-thirds of all adults who have hypertension or receive treatment with BP lowering medication at 30 years of age have a ~40 % higher risk of experiencing a CVD event than their age-matched and sex-matched counterparts with a lower level of BP. In addition, CVD events in individuals with hypertension tend to manifest about five years earlier than in individuals with a lower level of BP (Rapsomaniki et al, 2014)[35].



Pathophysiology

BP is determined by several parameters of the cardiovascular system, including blood volume and cardiac output (the amount of blood pumped by the heart per minute) as well as the balance of arterial tone that is affected by both intravascular volume and neurohumoral systems (discussed in the following sections). The maintenance of physiological BP levels involves a complex interplay of various elements of an integrated neurohumoral system that includes the renin-angiotensin-aldosterone system (RAAS), the role of natriuretic peptides and the endothelium, the sympathetic nervous system (SNS) and the immune system (figure 1). Malfunction or disruption of factors involved in BP control in any of these systems can directly or indirectly lead to increases in mean BP, BP variability or both, over time resulting in target organ damage (for example, left ventricular hypertrophy and CKD) and CVD outcomes (Hall and Hall, 2018)[37].

Figure 1: **The main neuroendocrine systems involved in the regulation of blood pressure (**Neurohumoral, immune and organ systems involved in the maintenance of blood pressure. BP: Blood pressure, RAAS: renin-angiotensin-aldosterone system)

The pathophysiological mechanisms responsible for hypertension are complex and act on a genetic background. Primary hypertension involves multiple types of genes; some allelic variants of several genes are associated with an increased risk of developing primary hypertension and are linked in almost all cases to a positive family history. This genetic predisposition, along with a host of environmental factors, such as high Na^+ intake, poor sleep quality or sleep apnoea, excess alcohol intake and high mental stress, contribute to the development of hypertension (Gangwisch, 2014; Palagini et al, 2013)[38,39].

Finally, the probability of developing hypertension increases with aging, owing to progressive stiffening of the arterial vasculature caused by, among other factors, slowly developing changes in vascular collagen and increases in atherosclerosis (Mikael et al, 2017)[40].

Immunological factors can also play a major part, especially on the background of infectious or rheumatological diseases such as rheumatoid arthritis. The mosaic theory of hypertension describes its multifaceted pathophysiology (Harrison et al, 2013)[41].

Sodium (Na^+) is a crucial regulator of blood volume: high serum Na^+ concentration promotes fluid (water) retention, thereby increasing blood volume and BP. When dietary Na^+ increases in normotensive individuals, compensatory hemodynamic changes occur to maintain constant BP. These changes include reduction in renal and peripheral vascular resistance and increased production of nitric oxide (a vasodilator) from the endothelium. However, if the effect of nitric oxide is impaired or absent, an increase in BP occurs. Endothelial dysfunction is a risk factor for the development of salt sensitivity and subsequent hypertension. Salt sensitivity is defined as a marked elevation in BP following a Na^+ load of $\geq$5 g and is characterized by an elevation of systolic BP of at least 10 mmHg within a few hours of ingestion. Salt sensitive individuals have underlying endothelial dysfunction due to genetic or environmental influences. In response to a high salt load these individuals generally manifest overproduction of transforming growth factor β (TGF-β), which increases the risk of fibrosis, and oxidative stress, and have limited bioavailable nitric oxide. Chronic high salt ingestion can result in endothelial dysfunction, even in salt-resistant individuals and also affects the gut microbiota, with resultant changes that contribute to increased salt sensitivity and the development of hypertension (Feng et al, 2017; Wilck et al, 2017)[42,43].

The RAAS has wide-ranging effects on BP regulation, mediating Na^+ retention, pressure natriuresis (that is, the mechanism whereby increases in renal perfusion pressure (the gradient

between renal arterial and venous blood pressure) lead to decreased Na^+ reabsorption and increased Na^+ excretion), salt sensitivity, vasoconstriction, endothelial dysfunction and vascular injury, and plays an important part in the pathogenesis of hypertension (Hall and Hall, 2018)[37].

Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) play an important part in salt sensitivity and hypertension. They have important natriuretic and vasodilator properties that allow maintenance of Na^+ balance and BP during Na^+ loading (Kerkelä et al, 2015)[44].

Upon administration of a Na^+ load, Atrial and ventricular stretch leads to release of ANP and BNP, respectively, which leads to systemic vasodilation and decreased plasma volume (owing to fluid shifts from the intravascular to the interstitial compartment) and results in BP lowering (Curry, 2005)[45].

Natriuretic peptides increase glomerular filtration rate via an increase in efferent arteriolar tone in volume-expanded states and inhibit renal Na^+ reabsorption through both direct and indirect effects. Direct effects include decreased activity of Na^+-K^+-ATPase and the sodium-glucose co-transporter in the proximal tubule and inhibition of the epithelial sodium channel in the distal nephron. Indirect effects include inhibition of renin and aldosterone release (Woodard and Rosado, 2008)[46].

The endothelium is a major regulator of vascular tone and major contributor to salt sensitivity through NO. Endothelial cells produce a host of vasoactive substances, of which NO is the most important in BP regulation (KhaddajMallat et al, 2017)[47].

NO is continuously released by endothelial cells in response to flow-induced shear stress, leading to vascular smooth muscle relaxation through activation of guanylatecyclase and generation of intracellular cyclic guanosine monophosphate.

Interruption of NO production via inhibition of constitutively expressed endothelial NO synthase (eNOS) causes BP elevation and development of hypertension in animals and humans. Studies to evaluate NO activity in humans have demonstrated decreased whole-body production of NO in patients with hypertension compared with normotensive controls (Ayub et al, 2011; Panza et al, 1993)[48,49].

Insulin signaling

Insulin is a potent anabolic hormone that exerts a variety of effects on many types of cells. Some of the main metabolic actions of insulin are stimulating glucose uptake in skeletal muscles and adipocytes, promoting glycogen synthesis in skeletal muscles, suppressing hepatic glucose production, and inhibiting lipolysis in adipocytes (Janus et al, 2016)[50].

After ingestion, insulin is secreted from the pancreas and induces the uptake of circulating glucose in its target tissues by binding to an insulin receptor. This binding activates receptor autophosphorylation, which triggers a downstream signaling cascade through the phosphorylation of tyrosine residues of the insulin receptor substrates, IRS (IRS-1 or IRS-2), followed by phosphorylation of phosphatidylinositol 3-kinase (PI3K), phosphoinositide dependent kinase-1, Akt (Akt1 and Akt2), protein kinase C (PKC) and mammalian target of rapamycin (mTOR), as well as ribosomal protein S6 kinase beta 1 (S6K1) (Janus et al, 2016; Scott et al, 1998)[50,51].

These events result in an increased translocation of the glucose transporter 4 (GLUT4) to the membrane, thus facilitating glucose uptake. After uptake, free glucose is rapidly phosphorylated to glucose 6-phosphate (G6P), which subsequently enters different metabolic pathways (Bogan, 2012)[52].

On the other hand, insulin signaling enhances lipid storage in adipocytes by two mechanisms, by stimulating triacylglycerol synthesis and by inhibiting lipolysis. Triglycerides are stored in lipid droplets, which contain lipid droplet proteins, including perilipin (Choi et al, 2010)[53].

The inhibition of lipolysis occurs through the reduction of cAMP levels and the inhibition of protein kinase A (PKA) activity, hence attenuating HSL (hormone-sensitive lipase) phosphorylation and perilipin, causing a decline in the lipolysis rate. Nutritional needs change during exercise and starvation; triglycerides within the adipocyte lipid droplets are hydrolyzed to fatty acids, acylglycerides and glycerol by activating HSL (Czech et al, 2013)[54].

In the liver, insulin inhibits glucose production and release, by blocking gluconeogenesis and glycogenolysis through the regulation of expression of phosphoenolpyruvate carboxylase (PEPCK) (Shulman, 2000)[55]. Furthermore, insulin can stimulate glycogen synthesis through Akt2 activation, glycogen synthase kinase 3 (GSK3) inhibitions, and glycogen synthase (GS)

activation via desphosphorylation of serine residues at both the NH2 and COOH-terminals of these proteins (Hojlund, 2014)[56].

On the other hand, the vascular actions of insulin are complex, which may have either protective or deleterious effects on the vasculature. The protective effects are related to endothelial nitric oxide synthase (eNOS) activation via PI3K/Akt pathway. The deleterious effects involve the induction of vascular smooth muscle cell (VSMC) proliferation, vasoconstriction and proinflammatory activity. These vascular effects are mediated through the mitogen-activated protein kinase (MAPK) pathway, which is involved only in the mitogenic effects of insulin, but not in its metabolic effects (Kahn and Flier, 2000)[57].

Insulin resistance

Insulin resistance is defined as an experimental or clinical condition in which insulin exerts a biological effect lower than expected. This phenomenon is due to marked defects in the insulin-stimulated glucose uptake, particularly, in glycogen synthesis and, to a lesser extent, glucose oxidation. The effects of insulin resistance in different tissues depend on the physiological as well as metabolic function of the tissues. Due to their high metabolic demand insulin resistance has significant effects on skeletal muscle, adipocytes and liver tissue, which are the main targets of intracellular glucose transport as well as glucose and lipid metabolism (Dimitriadis et al, 2011)[58].

Skeletal muscle and adipocytes accounts for about 60–70% and 10% of insulin-stimulated glucose uptake respectively via the GLUT 4 receptors. Insulin resistance cause impaired glycogen synthesis and protein catabolism in skeletal muscles and inhibit lipoprotein lipase activity in adipocytes leading to an increased release of free fatty acids and inflammatory cytokines such as IL-6, TNFα, and leptin. Additionally, the liver accounts for 30% of insulin-stimulated glucose disposal and insulin resistance leads to impaired glucose output and fatty acid metabolism leading to increased triglyceride content and VLDL secretion from liver (Wilcox, 2005)[59].

Insulin resistance causes endothelial cell dysfunction by decreasing the production of nitric oxide from endothelial cells and increasing the release of pro-coagulant factors leading to platelet aggregation. In an insulin resistant state, the PI3K pathway is affected whereas the MAP kinase pathway is intact, which causes mitogenic effect of insulin in endothelial cells leading to atherosclerosis (Wu and Meininger, 2009)[60].

Interestingly, low levels of circulating insulin and insulin resistance have significant physiological roles in regulating metabolic adaptation during starvation and pregnancy. During starvation, low glucose levels leads to decreased secretion of insulin which facilitates the mobilization of glucose from liver, fatty acids and glycerol from adipocytes and amino acids from muscle tissue. These compensatory mechanisms help maintain blood glucose levels and utilization by vital systems like the brain and red blood cells (Berg et al, 2002)[61].

Insulin resistance is increased in pregnancy particularly from the second to third trimester. This ensures the adequate supply of metabolic substrates and nutrients to the fetus for its proper growth and development (Catalano, 2010)[62]. On the contrary, insulin resistance is a key player in the pathogenesis of metabolic diseases like type 2 diabetes and can be observed in several clinical conditions such as breast cancer, rheumatoid arthritis, polycystic ovary syndrome, non-alcoholic fatty liver disease and CVD (Williams et al, 2016; Lallukka and Yki-Jarvinen, 2016)[63,64].

The excess of lipids in the cardiomyocyte shunted into non-oxidative pathways results in the accumulation of toxic lipid species (lipotoxicity), which alters cellular signaling and cardiac structure. Disruptions in several cellular signaling pathways such as in mitochondrial dysfunction and endoplasmic reticulum stress have been associated with lipotoxicity. Mediators such as reactive oxygen species (ROS), nitric oxide (NO), ceramide, phosphatidylinositol-3-kinase, diacylglycerol (DAG), ligands of PPAR nuclear receptors, leptin have been proposed to promote these lipotoxic effects and enhances rates of apoptosis (Wende and Abel, 2010)[65].

Insulin Resistance and Hypertension

Insulin resistance is defined as a less than expected biologic response to a given concentration of the hormone and plays a pivotal role in the pathogenesis of T2D (Olefsky et al, 1973)[66]. For many years, the term insulin resistance has been associated exclusively with an inadequate effect of insulin on glucose metabolism and did not address other aspects of insulin action. However, insulin is a pleiotropic hormone and exerts a multitude of effects on lipid and protein metabolism, ion and amino acid transport, cell cycle, proliferation and differentiation, and nitric oxide (NO) synthesis (Fig. 2).

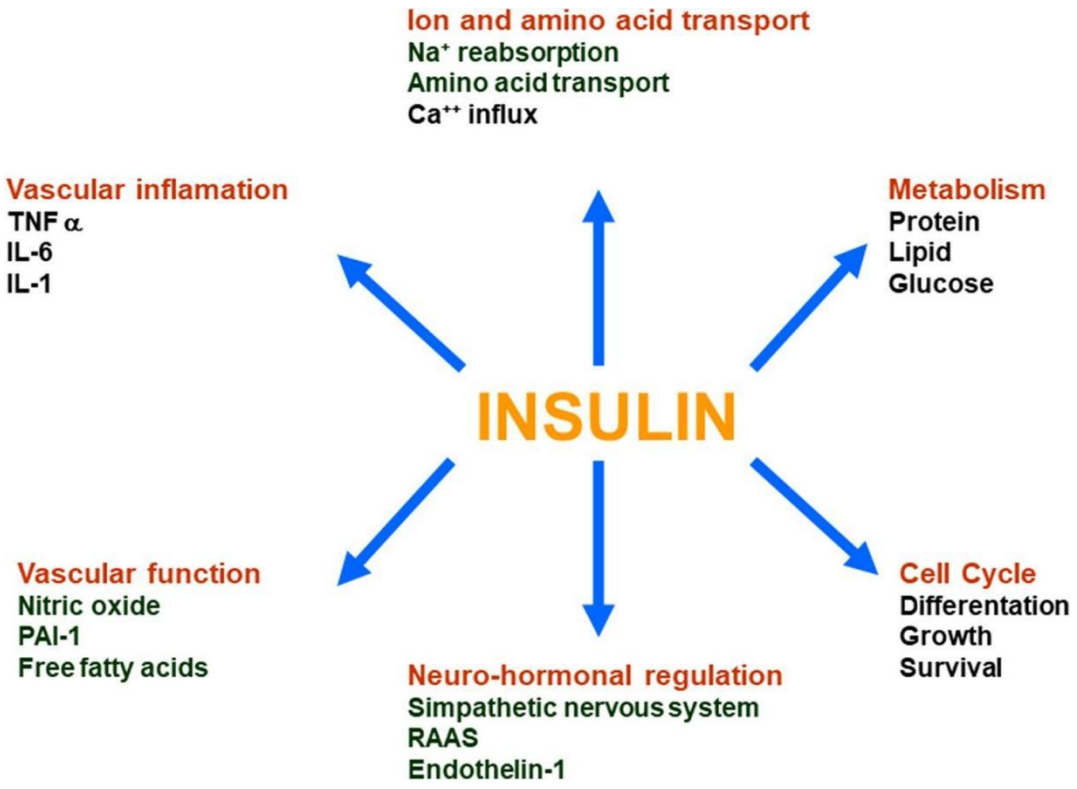


Fig. 2:

The pleiotropic action of insulin. Insulin regulates different physiological process including the glucose, protein and lipid metabolism, the cell cycle, growth and survival, the vascular tone and inflammation, the ions and amino-acid exchange/transport, and neurohormonal activity. Na+, sodium; Ca++, calcium; RAAS, Renin– angiotensin–aldosterone system; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; IL-1, interleukin-1; PAI-1, plasminogen activator inhibitor-1

In the context of the vascular system, insulin stimulation induces vasodilation through NO production and the state of insulin resistance impairs NO synthesis and vasodilation. Insulin resistance contributes to increase BP through several mechanisms, among which is the enhanced tissue angiotensin II (AngII) and aldosterone activities, the increased sympathetic nervous system activity and oxidative stress (Fukuda et al, 2001)[67].

However, emerging evidence indicate that endothelial dysfunction may represent the upstream event preceding peripheral reduction of insulin sensitivity, due to impairment of peripheral tissue blood flow. This phenomenon is known as “endothelial insulin resistance” and is mediated by increased oxidative stress, through a protein kinase C beta-dependent pathway. In fact, the suppression of reactive oxygen species-dependent pathways in the

endothelium has been shown to restore insulin delivery to peripheral organs by preserving NO availability (Tabit et al, 2010; Tabit et al, 2013)[68,69].

According to this view, endothelial loss of insulin signaling may represent an important mechanism linking hypertension to endothelial dysfunction. Molecular and pathophysiological mechanisms underlying the reciprocal relationship between insulin resistance and hypertension result in a vicious cycle which reinforces the link between metabolic and hemodynamic disorders. In fact, insulin resistance affects negatively myocardial energetic efficiency in hypertensive patients and in unselected population (Mancusi et al, 2017; Mancusi et al, 2019)[70,71].

The association between hypertension, insulin resistance, and resultant hyperinsulinemia is well documented. In untreated patients with essential hypertension, fasting and postprandial insulin levels are higher than in normotensive controls, with a direct correlation between plasma insulin concentrations and BP. Interestingly, the association of insulin resistance and essential hypertension does not occur in secondary hypertension (Reaven et al, 1996)[72].

Of note, insulin resistance and hyperinsulinemia also exist in rats with genetic hypertension such as Dahl hypertensive and spontaneously hypertensive rat (SHR) strains. Altogether these data suggest the existence of a common genetic pathway for essential hypertension and insulin resistance, a concept that is also supported by the finding of altered glucose metabolism in normotensive offspring of hypertensive patients (Grunfeld et al, 1994)[73].

The common genetic background of insulin resistance and hypertension is further supported by the discovery of specific genetic abnormalities in people with combinations of insulin resistance, obesity, dyslipidemia, and hypertension. These defects include a mutation of the β3-adrenergic receptors (ARs), which regulates lipolysis in visceral fat, and the presence of two mutated genes on chromosome 7q, one that controls insulin levels and BP and the other, leptin, a peptide that regulates food intake. Deficiency in CD36, a known fatty acid transporter, is also believed to be involved in the predisposition to insulin resistance and hypertension in Asians (Miyaoka et al, 2001)[74].

The relationship between insulin resistance and hypertension is a complex and multifactorial phenomenon which involves both genetic basis and environmental factors. In the western countries, sedentary life style and hyper caloric food intake are endemic behaviors which play a key role in the development of insulin resistance, mainly through epigenetic modifications. In particular, DNA methylation, histone modifications and noncoding RNA activity (miRNA) are the principal mechanisms that alter the protein transcription and expression, which, in turn, modify the cellular phenotype. The translocation of GLUT 4 to the cell membrane is the

principal step of insulin-induced glucose uptake. Insulin resistance state is characterized by lower expression levels and impaired translocation of GLUT 4. Experimental data indicate that the mutilation of DNA, induced by over nutrition during fetal life, decreases the gene expression of proteins involved in insulin signal transduction, like GLUT 4. The expression of GLUT 4 is also affected by mi RNA.

In particular, in myocytes the miRNA 106b impairs insulin signalling by decreasing insulin-stimulated translocation of GLUT 4. Mitochondrial dysfunction, which also plays a key role in the genesis of insulin resistance, is affected by epigenetic modifications. In particular, methylation of the gene encoding for peroxisome proliferator-activated receptor alpha (PPARα) has been reported in obese subjects. These data reinforce the hypothesis that epigenetic modifications are at least partially responsible for the link between behavior habits and insulin resistance (Dos Santos et al, 2015)[75].

Insulin Resistance Directly Affects Blood Pressure Control

In healthy subjects, insulin evokes a net reflex in sympathetic outflow and at the same time it blunts the vasoconstrictive effect resulting from this sympathetic activation. On the contrary, in hypertensive patients insulin evokes a sympathetic activation that is three times greater than in normal subjects, and moreover its vaso-relaxant action is impaired (Lembo et al, 1992)[76]. This mechanism is involved in deregulation of peripheral vascular resistance, which contributes to increase BP levels (Fig. 3). The key role of insulin resistance in the pathogenesis of hypertension has been further supported by the evidence that in aortic rings of SHR the resistance to the vascular action of insulin is already present at the age of 5 weeks, before the onset of arterial hypertension, suggesting that in SHR vascular resistance to insulin action is specific and not related to the compensatory hyperinsulinemia or hyperglycemia (Lembo et al, 1995)[77]. On the other hand, we have demonstrated, in rats fed for 6 months with hypercaloric diet that the increase of BP and the development of LVH are associated with both hyperinsulinemia or hyperglycemia. In addition, insulin resistance and the resultant hyperinsulinemia are involved in the development of hypertension-related TOD, through the abnormalities of the counter-regulatory effects of insulin. In particular, impairment of cell membrane ion exchange, enhanced sympathetic nervous and renin-angiotensin systems, suppressed atrial natriuretic peptide activities, sodium retention, and plasma volume expansion contribute to the development of chronic kidney disease, LVH, CA.

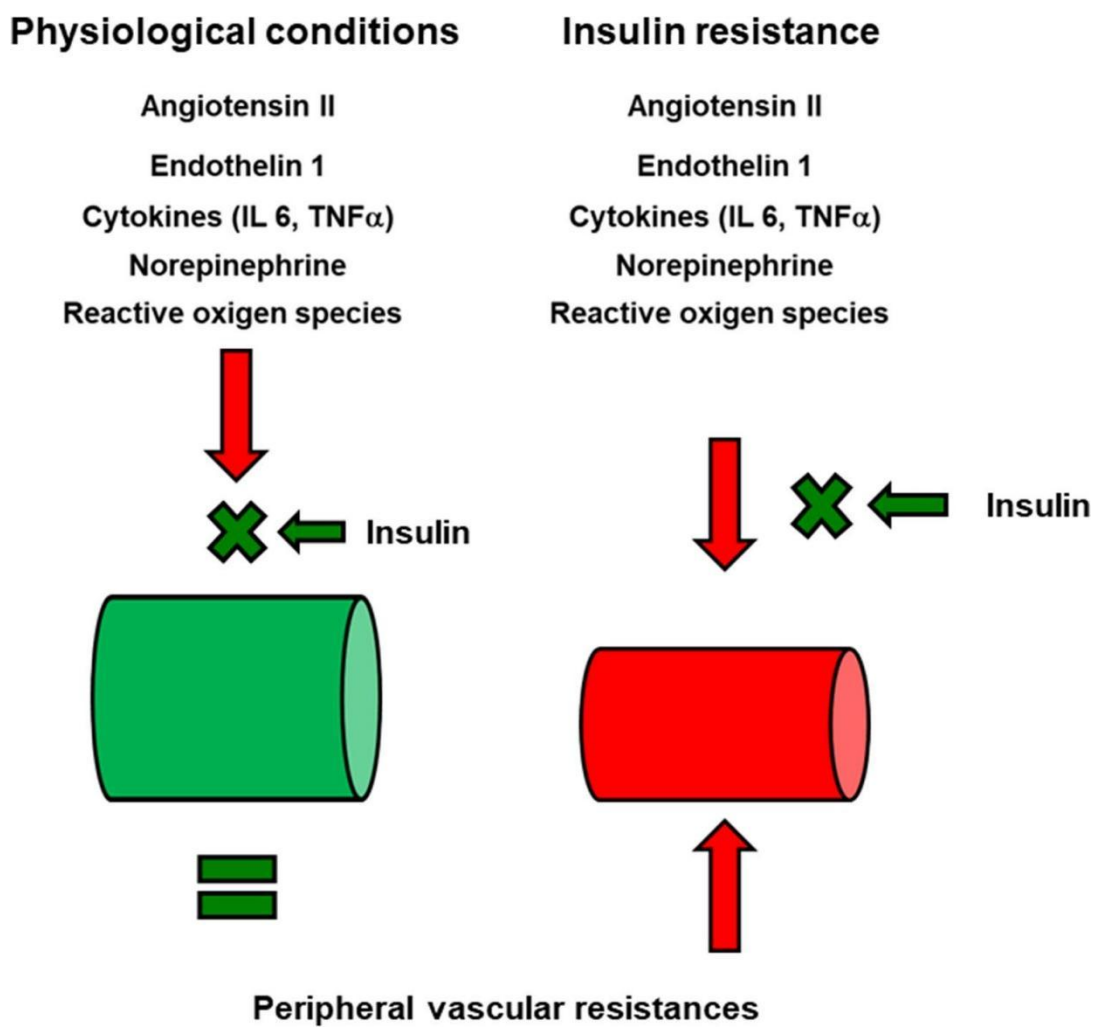


Fig.3 : Regulation of peripheral vascular resistances by insulin and effects of insulin resistance. In physiological conditions, insulin antagonizes (green arrows) the effects of vasoconstrictor mediators (red arrows), contributing to maintain the normal vascular tone. Insulin resistance (red arrows), impairs the capability of insulin to counterbalance the action of vasoconstrictor mediators, resulting in the increase of vascular peripheral resistances. TNF-α, tumor necrosis factor-α; IL-6, interleukin-6

Comparative studies

Sinha et al (2015)[78] observed the insulin resistance in adult male with essential hypertension. The study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka, Bangladesh from July 2012 to June 2013. A total number of 150 male subjects were selected with age ranging from 25-45 years. Seventy-five male essential hypertensives were enrolled from Out- patient Department of Medicine, Dhaka Medical College Hospital, Dhaka. Otherwise, healthy 75 of similar age were studied as control. Insulin resistance was assessed by HOMA-IR method. Fasting serum insulin level was measured by ELISA and fasting blood

glucose by glucose oxidase method. The study revealed that essential hypertension has positive and significant relationship with fasting serum insulin level and insulin resistance. The authors concluded that the incidence of insulin resistance was higher in essential hypertensive subjects in comparison to the control subjects. More in-depth prospective research was advocated to find remedies for common Bangladeshi patients.

deMorais et al (2016)[80] evaluated the correlation of blood pressure with insulin resistance, waist circumference and body mass index in adolescents. Cross-section study was conducted on a representative sample of adolescent students. One group of adolescents with altered blood pressure detected by casual blood pressure and/or home blood pressure monitoring (blood pressure > 90^{th} percentile) and one group of normotensive adolescents were studied. Body mass index, waist circumference were measured, and fasting glucose and plasma insulin levels were determined, using the HOMA-IR index to identify insulin resistance. A total of 162 adolescents (35 with normal blood pressure and 127 with altered blood pressure) were studied; 61% (n = 99) of them were boys and the mean age was 14.9 ± 1.62 years. Thirty-eight (23.5%) adolescents had altered HOMA-IR. The group with altered blood pressure had higher values of waist circumference, body mass index and HOMA-IR ($p< 0.001$), and such correlation was stronger than in the normotensive group. There was also a significant moderate correlation between waist circumference and HOMA-IR in both groups ($\rho = 0.345$; $p < 0.05$). Logistic regression showed that HOMA-IR was as predictor of altered blood pressure (odds ratio − OR = 2.0; $p = 0.001$). The study concluded that there was a significant association of insulin resistance with blood pressure and the impact of insulin resistance on blood pressure since childhood. The correlation and association between markers of cardiovascular diseases was more pronounced in adolescents with altered blood pressure, suggesting that primary prevention strategies for cardiovascular risk factors should be early implemented in childhood and adolescence.

Hussain and Tripathi (2017)[81] evaluated the correlation between insulin resistance, metabolic syndrome and their associated factors in hypertensive patients. The study was conducted on 100 patients who attended to the Department of Medicine, NSCB Medical College, Jabalpur, Madhya Pradesh, India. 50 patients of both sexes having essential hypertension were participated in the study and considered as hypertensive group. Other healthy 50 patients of similar sex and age group were studied as control group (normotensive) for comparison. Insulin resistance was estimated by using homeostasis model assessment (HOMA-IR) method. Mean age of the patients of hypertensive group was 49.79±17.04 years and mean age

of normotensive group was 51.94±16.64 years. Male preponderance was observed in both the groups. Out of 50 from each group, 19 (38%) of hypertensive patients and 7 (14%) of normotensive patients had insulin resistance. Metabolic syndrome was noted in 23 (46%) and 10 (20%) cases of hypertensive and normotensive groups respectively and this difference was found to be statistically significant (p=0.01). The mean fasting and post prandial blood sugar levels were almost similar in both groups (p=0.03). Mean total cholesterol levels were significantly lower in hypertensive groups than that of normotensive group (p=0.03). The mean serum insulin levels were high in hypertensive groups than that of normotensive group which was statistically significant (p=0.00). Mean HOMA-IR, waist size and waist hip ratio (WHR) was significantly (p=0.02) higher in hypertensive group than that of control group. The study concluded that results of the study supported the strong correlation between insulin resistance and essential hypertension and also confirmed that insulin resistance was the major risk factor of metabolic syndrome.

Rad et al (2020)[82] investigated the relationship between hypertension and insulin resistance in non-diabetic participants who were referred to Qazvin Metabolic Diseases Center. 1103 participants (111 non-diabetic with newly diagnosed hypertension and 992 normotensive subjects aged ≥ 20 years) were enrolled from September 2014 to April 2016 in Qazvin (Iran). Systolic and diastolic blood pressure, insulin resistance, waist circumference, body mass index, triglycerides, cholesterol, LDL-cholesterol, fasting blood glucose (FBG) were measured. Fasting triglyceride to high density lipoprotein cholesterol ratio (TG/HDL-C) was used as a surrogate of insulin resistance. Ten percent of all participants had hypertension. TG/HDL-C was 3.78 ± 3.28 in non-HTN and 5.76 ± 5.35 in HTN participants ($p < 0.001$). The frequency of all cardio-metabolic risk factors (except HDL cholesterol level) was higher in hypertensive group, after adjusting for age and gender ($p < 0.001$). The study concluded that essential hypertension was associated with a higher prevalence of hyperinsulinemia and insulin resistance in the non-diabetic community in Iran.

Quesada et al (2021)[83] examined the associations of insulin resistance, quantified by homeostasis model assessment of insulin resistance (HOMA-IR), with systolic BP (SBP) and diastolic BP overall and stratified by sex and prediabetes status in unadjusted and adjusted analyses. The total sample included 52% women; mean (SD) age, 37.2 (13.4) years; 39% of participants had prediabetes (mean [SD] HOMA-IR, 2.8 [2.2]). Stage 1 or 2 hypertension was present in 26% of participants (mean [SD] SBP, 116.8 [15] mmHg and diastolic BP, 71.0 [10.4] mmHg). Overall, there was a significant linear association between HOMA-IR and

both SBP (β, 2.64±0.44) and diastolic BP (β, 1.49±0.35). They found a significant interaction with sex and the association between HOMA-IR and SBP; the association was linear in men and nonlinear in women. There was no statistically significant interaction between prediabetes status and the associations between HOMA-IR and BP. They concluded that in a large community based sample of Hispanic/Latino adults of diverse national backgrounds not taking antihypertensive medications and free from diabetes, insulin resistance was positively associated with both SBP and diastolic BP.

Wang et al (2022)[84] investigated the correlations between different blood pressure levels and different degrees of insulin resistance, as well as their interactions, with newly diagnosed diabetes mellitus. They conducted a retrospective study on 1251 adult medical examiners who were examined in the Physical Examination Center of Zhongshan Hospital, Fudan University (Shanghai, China) during 2015. All human subjects had no history of diabetes. General clinical data, including blood pressure, fasting glucose and 2-h post-load glucose levels, and lipid profiles, were collected. HOMA-IR was separately calculated. s. In 1251 physical examination subjects, a total of 166 cases of newly diagnosed diabetes were detected, with a total detection rate of 13.3%. The rates of newly diagnosed diabetes in the normal blood pressure group, high-normal blood pressure group, and hypertension group were 4.9%, 10.6%, and 19.0%, respectively. Compared with the normal blood pressure group, the proportion of newly diagnosed diabetes in the hypertension group was significantly increased [OR: 2.956, 95% CI 1.736-5.032, P < 0:001]. According to the stratification of HOMA-IR level, with the first quartile group (HOMA-IR< 0:001]. When hypertension was combined with insulin resistance (HOMA-IR ≥2.68), the risk of newly diagnosed diabetes was 38.32 times compared with the control group [OR: 38.315, 95% CI 9.227-159.108, P < 0:001]. The authors concluded that elevated blood pressure levels and insulin resistance levels were associated with the risk of newly diagnosed diabetes. Hypertension was an independent risk factor for newly diagnosed diabetes, and the combination of hypertension with insulin resistance further increased the risk of newly diagnosed diabetes.

Gu et al (2022)[85] explored the association between three IR indicators and ISH among young and middle-aged adults with normal fasting plasma glucose (NFG). This large cross-sectional study included 8246 young and middle-aged men with NFG and diastolic blood pressure< 90 mmHg. The homeostasis model assessment for IR (HOMA-IR) index, triglyceride glucose (TyG) index, and the metabolic score for IR (METS-IR) were calculated with the

corresponding formula. The proportions of ISH among young and middle-aged men were 6.7% and 4.4%, respectively. After fully adjusting, only HOMA-IR rather than TyG and METS-IR was significantly associated with ISH. Moreover, fully adjusted smooth curve fitting showed that the association between HOMA-IR and ISH were approximately linear in both two age groups (P for non-linearity were 0.047 and 0.430 in young and middle-aged men, respectively). Among young and middle-aged men with NFG, using HOMA-IR instead of noninsulin-dependent IR indicators might have advantages in the hierarchical management of ISH.

Lin et al (2022)[86] investigated how different cutoffs of hypertension affect the association of hypertension to incident diabetes and the progression of insulin resistance. A total of 1177 subjects without diabetes at baseline were followed for 4.5 years. Diabetes was diagnosed by the results of oral glucose tolerance tests and HBA1c, or if anti-diabetic agents were used. Hypertension by both criteria was associated with incident diabetes. Change of HOMA2-IR every 5 years (DHOMA2-IR/5 yr) was higher in subjects with hypertension than those without (adjusted p= 0.044). Subjects with treated hypertension had the highest risk of diabetes (HR 2.98, $p < 0.001$) and DHOMA2-IR/5 yr, compared with subjects with normal blood pressure. However, the associations of hypertension, HR of incident diabetes and DHOMA2- IR/5 yr were attenuated by the 2017 ACC/AHA criteria, as compared with that by the JNC7 and 2018 ESC/ESH criteria. The authors concluded that hypertension by both criteria was associated with incident diabetes and accelerated progression of insulin resistance, and the associations were attenuated by the 2017 ACC/AHA criteria.

Han et al (2022)[87] investigated the association between the novel non–insulin-based metabolic score for insulin resistance (METS-IR) index and pre-hypertension (HTN) or HTN in normoglycemia Japanese participants. The NAGALA medical examination program at Murakami Memorial Hospital in Gifu, Japan was found in 1994. 15,453 participants enrolled in this program from 2004 to 2015 was included in the retrospective study to explore the association between the METS-IR index and pre-HTN or HTN. Covariates included serum biomarkers and clinic demographic characteristics. Logistic regression was applied to explore the association between METS-IR level and pre-HTN or HTN. The study included a total of 15453 participants. The prevalence rates of preHTN and HTN were 28.55% (4412/15453) and 6.23% (962/15453), respectively. Adjusted for confounding factors in the multivariable logistic regression analysis models, when METS-IR was used as a categorical variable, high METS-IR was significantly associated with both pre-HTN (adjusted odds ratio (OR) = 1.95,

95% confidence interval (CI): 1.61–2.36) and HTN (adjusted OR = 2.12, 95% CI: 1.44–3.11). When METS-IR was used as a continuous variable, each 1 unit increase in METS-IR was associated with a 7% increase in the prevalence of pre-HTN (adjusted OR = 1.07, 95% CI: 1.06–1.08) and with a 13% increase in the prevalence of HTN (adjusted OR = 1.13, 95% CI: 1.10–1.16). Stratified analyses indicated a positive correlation between METS-IR and pre-HTN or HTN in normoglycemia subjects with different characteristics. The study concluded that METS-IR levels were significantly associated with pre-HTN or HTN in normoglycemia individuals in Gifu, Japan. METS-IR might be used as a monitoring indicator for the development of HTN primary prevention and management strategies in the future, but it still needed more research to confirm.

MATERIAL AND METHODS

Study Place: The study was conducted in Department of Medicine, Santosh Medical College and hospital, Ghaziabad

Study Design: Cross-sectional Observational Study

Study frame: Study was done in all hypertensive and non-hypertensive population who attended Medicine OPD and IPD of Santosh Hospital.

Inclusion criteria:

- Study population attended medicine OPD and IPD.
- Age $\geq$ 40 years
- Both genders were included
- Known case of hypertension or newly diagnosed hypertension and normotensive population.

Exclusion criteria:

- Failure to obtain informed consent
- Age <40 years
- Recent myocardial infarction (within last 6 months)
- Recent stroke (within last 6 months)
- Recent surgery (within last 6 months)
- Chronic liver disease
- Exclusion of secondary hypertension by history taking and general physical examination

Sample size

In this study, as we want to study relationship of hypertension with insulin resistance. Therefore, in order to calculate the sample size, we need to have the estimated prevalence of hypertension as well as the prevalence of insulin resistance in hypertensive patients.

To this reference, we have found that past researches have reported the prevalence of hypertension in India equivalent to 29.8%. Also, a research work suggested that the prevalence of insulin resistance in hypertensive patients was 50.9%. On calculating the sample size, using these values and the sample size formula with the correction factor by Fleiss given below:

$$n_1 = \frac{\left[(Z_{\frac{\alpha}{2}}\sqrt{(r+1)\bar{p}\bar{q}} + Z_{1-\beta}\sqrt{(rp_1q_1 + p_2q_2)}\right]}{r(p_1 - p_2)^2}$$

$$\text{And } n_2 = rn_1$$

Where

n_1= number of exposed

n_2= number of unexposed

$Z_{\frac{\alpha}{2}}$= standard normal deviate for two-tailed test based on alpha level (relates to the confidence interval level)

$Z_{1-\beta}$=standard normal deviate for one-tailed test based on beta level (relates to the power level)

r= = ratio of unexposed to exposed

p_1= proportion of exposed with disease and $q_1 = 1 - p_1$

p_2= proportion of unexposed with disease and $q_2 = 1 - p_2$

$\bar{p} = \frac{p_1 + rp_2}{r+1}and\bar{q} = 1 - \bar{p}$

For the Fleiss method with the correction factor, take the sample size from the uncorrected sample size formula and place into the following formula:

$$n_{1cc} = \frac{n_1}{4}\left[1 + \sqrt{1 + \frac{2(r+1)}{n_1 r|p_2 - p_1|}}\right]$$

Sample Size:X-Sectional, Cohort, & Randomized Clinical Trials			
Two-sided significance level(1-alpha):			95
Power(1-beta, % chance of detecting):			80
Ratio of sample size, Unexposed/Exposed:			1
Percent of Unexposed with Outcome:			30
Percent of Exposed with Outcome:			51
Odds Ratio:			2.4
Risk/Prevalence Ratio:			1.7
Risk/Prevalence difference:			21
	Kelsey	**Fleiss**	**Fleiss with CC**
Sample Size – Exposed	87	86	95
Sample Size-Nonexposed	87	86	95
Total sample size:	174	172	190

Taking the sample size evaluated from Fleiss with CC formula and adjusting it for loss to follow up as 20%, we get the final sample size as 190 patients.

Subject Confidentiality:

Data collection was on paper. The patients participating in the study was contacted only by the persons involved in the study. All the patient specific data was kept in strict confidence. Patient identifiable data (name, contact, address, etc.) will not be presented in journal or any public forum.

Informed Consent:

Informed consent process was initiated prior to the individual agreeing to participate in the study and continuing through out the individual's study participation. The form provided had all the information required for the patient to understand their role in the study. It was in a language understandable by each member of the study population. It was submitted for the ethical committee clearance.

Financial Inputs and Funding:

All the study related procedures and investigations were done according to the institutional protocol. All these expenses were borne by the patient. Also, this study was not being sponsored by any pharmaceutical company.

METHODOLOGY:

Study Tools

- All the patients subjected to history taking and clinical examination to diagnose primary hypertension.
- Secondary hypertension excluded based on history taking , general physical examination and alcohol intake, drug intake (NSAID'S , corticosteroids, oral contraceptives),obesity, pregnancy, renal diseases (Glomerulonephritis, renal vascular disease and polycystic kidney disease),endocrine disorders (Acromegaly, hypothyroidism, thyrotoxicosis , hyperparathyroidism, Cushing syndrome, Conn syndrome, Pheochromocytoma).
- The primary hypertensive patients were subjected to evaluation of hypertension grades as per JNC-8 classification Guidelines as shown in the (table no.1)

Table no.1

Hypertension	**Systolic blood pressure (mm Hg)**	**Diastolic blood pressure (mm Hg)**
Normal	<120	<80
Pre-Hypertension	120-139	80-89
Stage 1 Hypertension	140-159	90-99
Stage 2 Hypertension	≥160	≥100

- The BP was taken in supine position after 5 minutes of rest in the left arm. Three readings were taken for each patient and mean of the three readings was taken as the BP reading. The higher reading of systolic and diastolic was considered for evaluation. The patientswere subjected to
- Plasma Lipid Profile – measured by Enzymatic Method-Cholesterol Oxidase-Peroxidase
- Renal Function Test – measured by Uricase and Jaffe method
- Fasting blood sugar – measured by Glucose Oxidase-Peroxidase Method
- Urine Albumin Creatinine Ratio (ACR) - measured by Immunoturbidimetric Method
- Fasting insulin – measured by Sandwich ELISA Test
- HOMA-IR (Homeostatic Model Assessment – Insulin Resistance) was calculated as Insulin resistance index[23](Fasting insulin (microU/L) x fasting glucose (nmol/L)/22.5)

Ethical Considerations:

The protocol of the present study was submitted to the Ethics Committee of Santosh Medical College & Hospital for review. After getting their approval the study was initiated in the institution. Also prior to enrolling any patient in the study, a voluntary written informed consent was obtained for participation.

Data management and Statistical Analysis:

- A comparison and contrast analysis of data was carried out using standard statistical methods.
- Quantitative data was analysed using a two-sample independent 't-test' and categorical data was analysed using 'Pearson's $\chi 2$-test/Fisher's exact test'.
- P-values less than 0.05 considered to be significant.
- All data expressed in mean ± SD.

RESULTS AND OBSERVATIONS

With hypertension: Cases; without hypertension: Controls.

The present study was conducted in Department of Medicine, Santosh Medical College and hospital, Ghaziabad with the objective to study relationship of hypertension with insulin resistance. A total of 95 cases and 95 controls were included in the study.

Table-2: Distribution of patients according to age

Groups	**Age in years (Mean±SD)**
With hypertension	53.74±8.29
Without hypertension	54.07±9.03
p-value[1]	0.78

[1]Unpaired t-test

Table-2 & Fig.1 shows the distribution of patients according to age. The mean age of patients of with and without hypertension was 53.74±8.29 and 54.07±9.03 years respectively. There was no significant (p>0.05) in age between with and without hypertension patients showing comparability of the groups in terms of age.

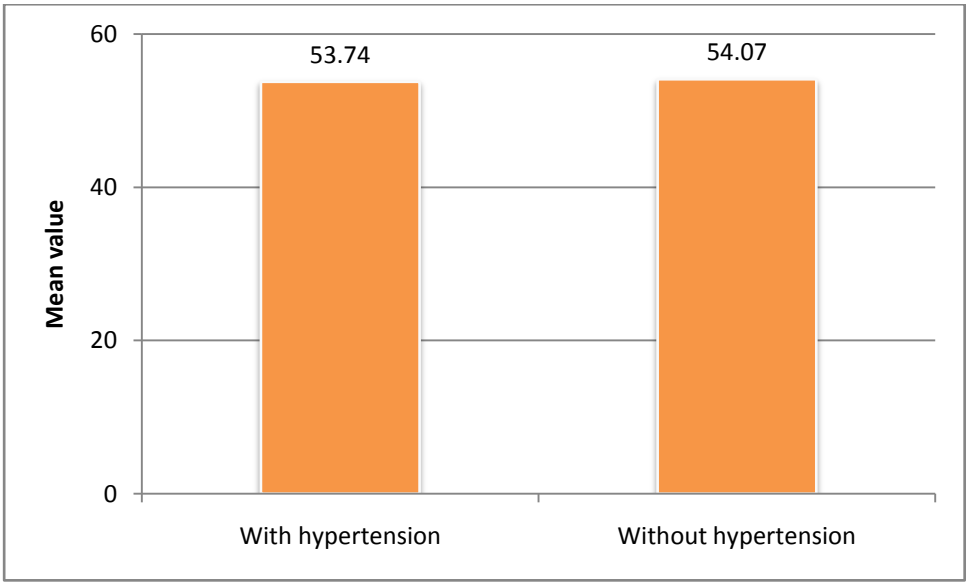


Fig. 1: Distribution of patients according to age

Table-3 : Distribution of patients according to gender

Gender	With hypertension (n=95)		Without hypertension (n=95)		p-value[1]
	No.	%	No.	%	
Male	42	44.2	42	44.2	1.00
Female	53	55.8	53	55.8	

[1]Chi-square test

Table-3& Fig.2 shows the distribution of patients according to gender. There were equal no. of male and females in both the groups.

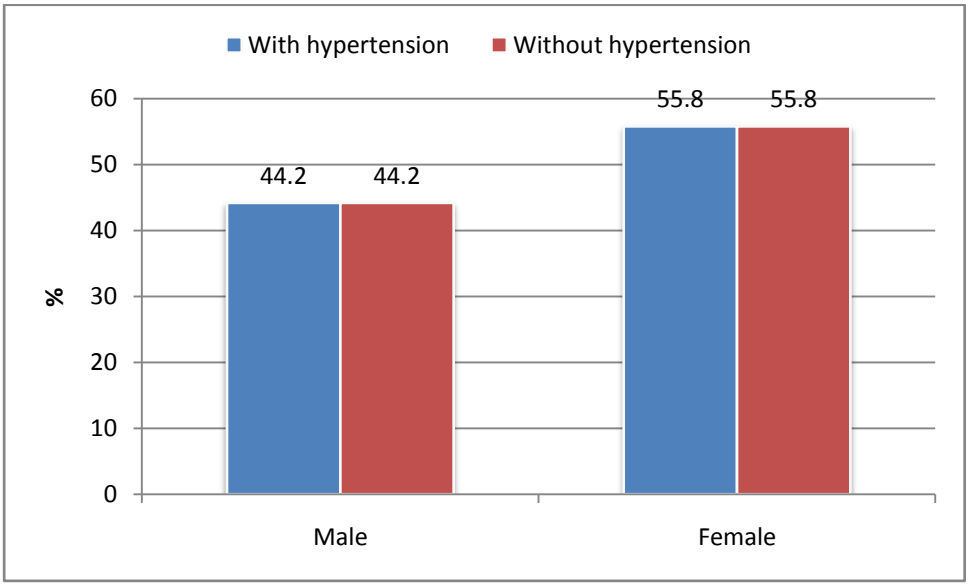


Fig. 2: Distribution of patients according to gender

Table-4: Distribution of patients according to BMI

Groups	BMI in kg/mtr^2 (Mean±SD)
With hypertension	22.67±2.87
Without hypertension	22.98±2.66
p-value[1]	0.78

[1]Unpaired t-test

Table 4& Fig.3 shows the distribution of patients according to BMI. The mean BMI of patients of with and without hypertension was 22.67±2.87 kg/mtr^2 and 22.98±2.66 kg/mtr^2 respectively. There was no significant (p>0.05) in BMI between with and without hypertension.

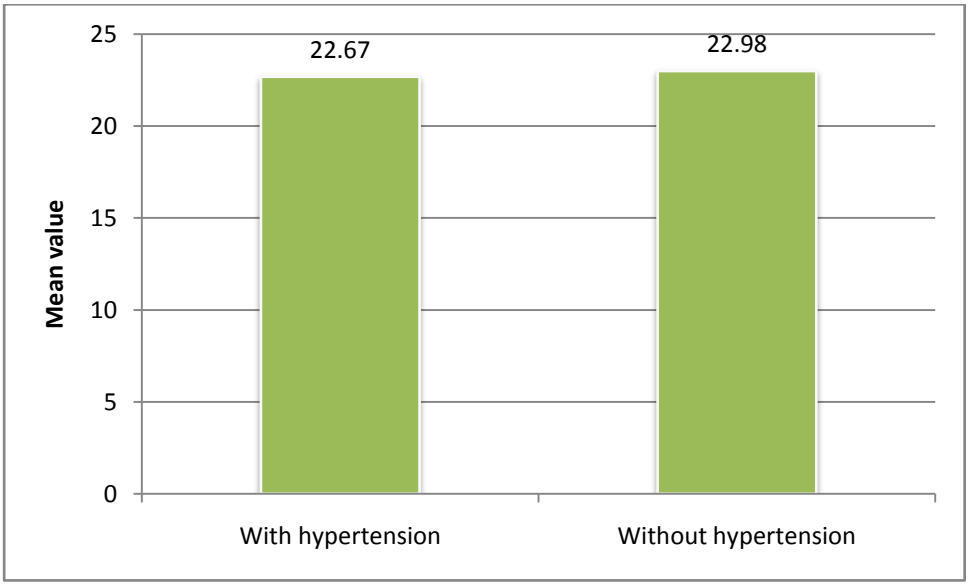


Fig. 3: Distribution of patients according to BMI

Table-5: Distribution of stage of hypertension among cases

Stage	No. (n=95)	%
Stage I	28	29.5
Stage II	67	70.5

Table-5& Fig.4 shows the distribution of patients according to stage of hypertension. Stage II hypertension was among majority of patients.

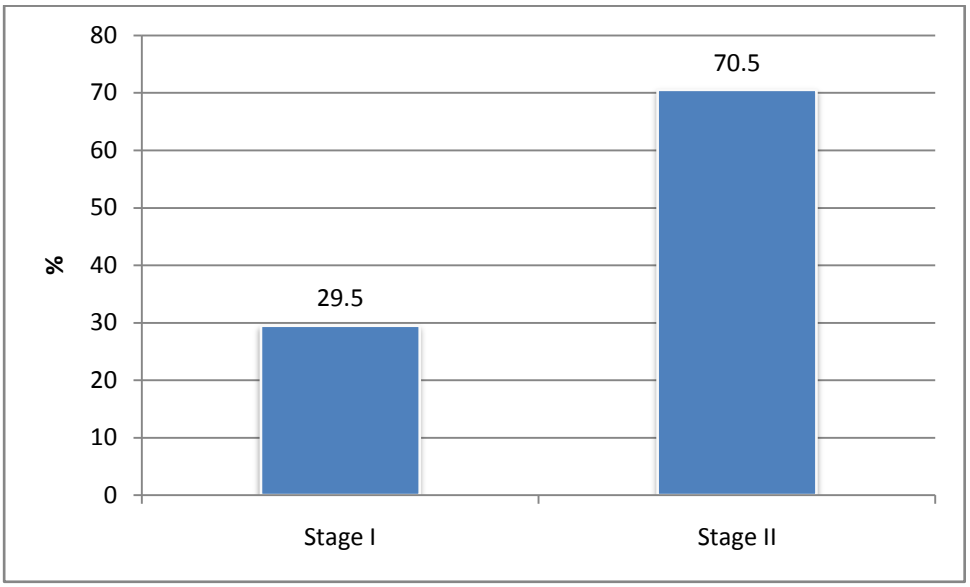


Fig. 4: Distribution of stage of hypertension among cases

Table-6: Comparison of urea and Creatinine with stage of hypertension

	Stage I	Stage II	p-value[1]
Urea (mg/dl)	36.32±8.14	32.99±7.70	0.06
Creatinine (mg/dl)	0.97±0.27	1.03±0.33	0.43

[1]Unpaired t-test

Table- 6& Fig.5 shows the comparison of urea and Creatinine with stage of hypertension. There was no significant (p>0.05) difference in urea and Creatinine between stage I and stage II hypertension.

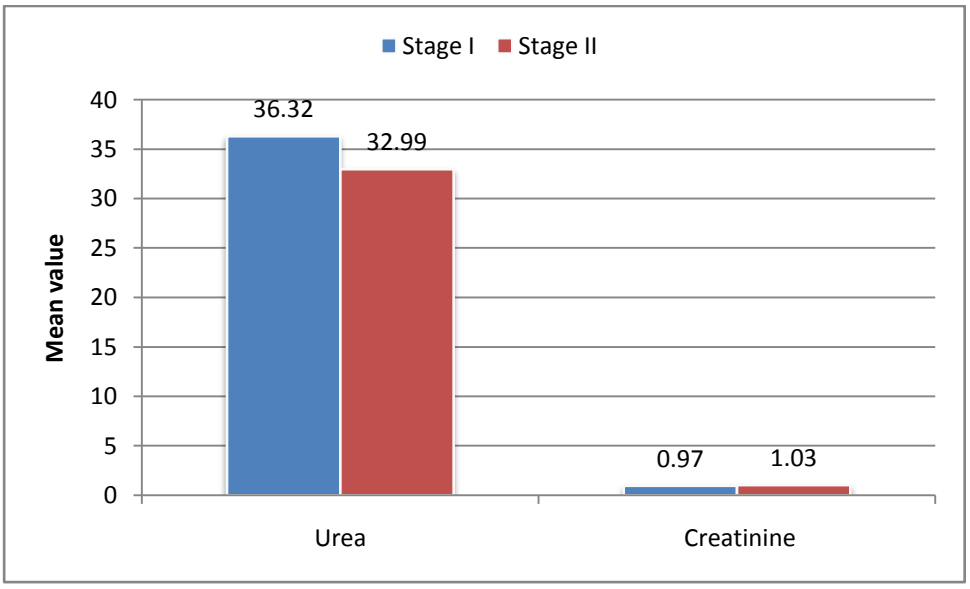


Fig. 5: Comparison of urea and Creatinine with stage of hypertension

Table-7: Comparison of ACR with stage of hypertension

Stage of hypertension	ACR (Mean±SD)
Stage I	27.32±27.11
Stage II	112.73±190.71
p-value[1]	0.01*

[1]Mann-Whitney U test, *Significant

Table-7& Fig.6 shows the comparison of ACR with stage of hypertension. ACR was significantly (p=0.01) higher patients of stage II hypertension (112.73±190.71) compared to stage I (27.32±27.11).

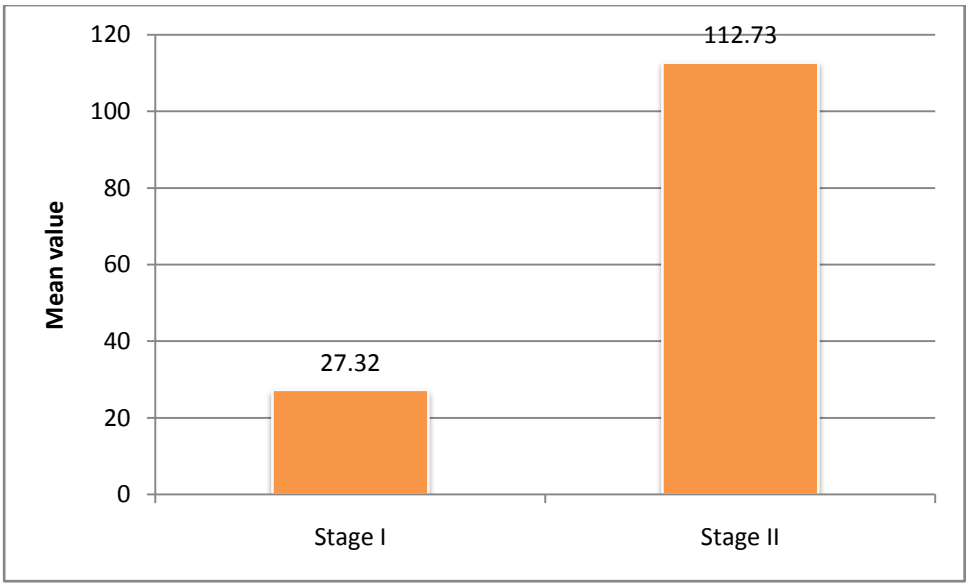


Fig. 6: Comparison of ACR with stage of hypertension

Table-8: Comparison of Lipid profile with stage of hypertension

Lipid profile	Stage I	Stage II	p-value[1]
TC	214.07±54.92	196.63±54.13	0.15
TG	178.86±95.96	155.49±75.91	0.21
LDL	118.71±55.47	113.57±47.51	0.64
HDL	40.57±6.54	43.55±15.01	0.31

[1]Unpaired t-test

Table-8& Fig.7 shows the comparison of lipid profile with stage of hypertension. There was no significant (p>0.05) difference in lipid profiles between with and without hypertension.

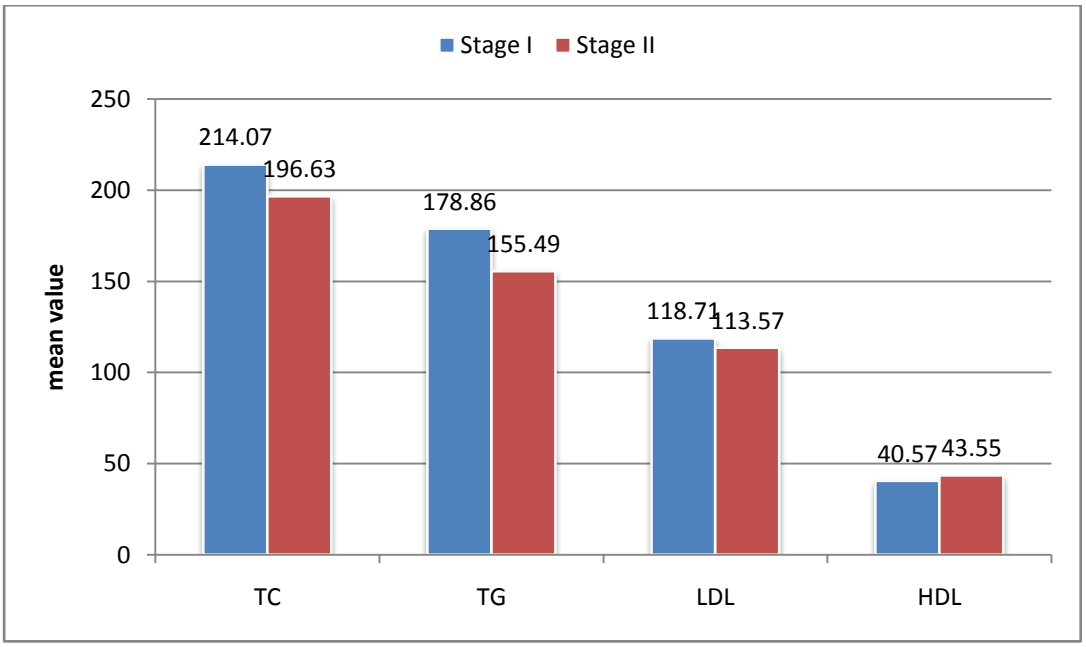


Fig. 7: Comparison of Lipid profile with stage of hypertension

Table-9: Comparison of FBS with stage of hypertension

Stage of hypertension	FBS (Mean±SD)
Stage I	92.89±12.12
Stage II	93.79±13.59
p-value[1]	0.76

[1]Mann-Whitney U test, *Significant

Table-9& Fig.8 shows the comparison of FBS with stage of hypertension. There was no significant (p>0.05) difference in FBS between with and without hypertension.

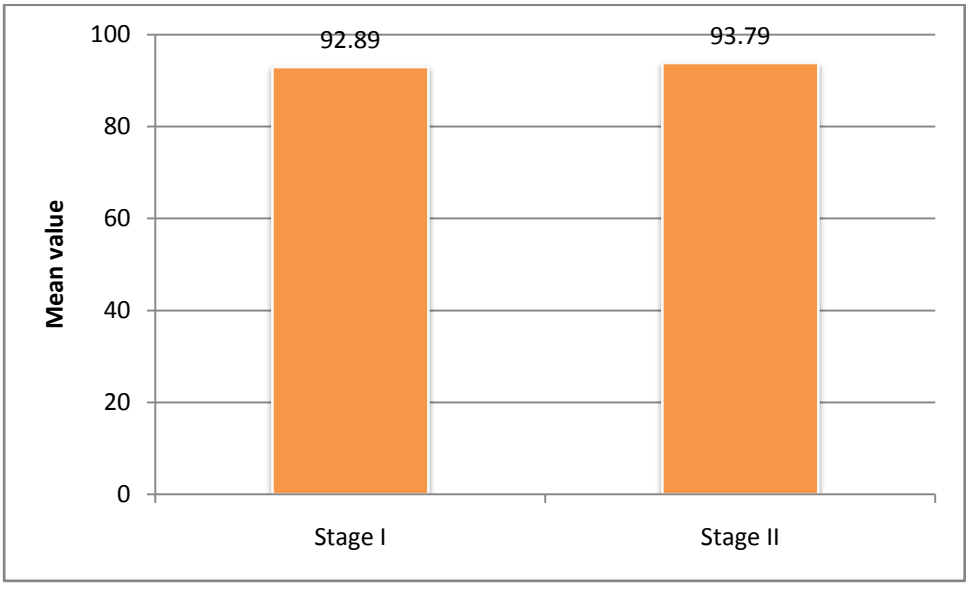


Fig. 8: Comparison of FBS with stage of hypertension

Table-10: Comparison of Serum insulin and HOMA with stage of hypertension

	Stage I	Stage II	p-value[1]
Serum insulin	35.39±22.57	31.45±20.60	0.41
HOMA	7.98±4.78	7.17±4.60	0.44

[1]Unpaired t-test

Table-10 & Fig.9 shows the comparison of serum insulin and HOMA with stage of hypertension. There was no significant ($p>0.05$) difference in serum insulin and HOMA between with and without hypertension.

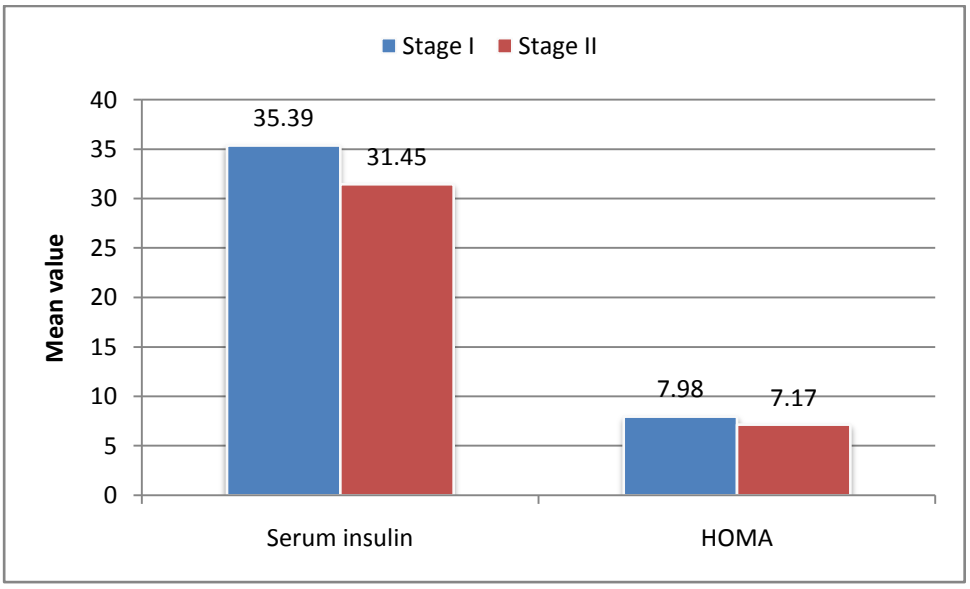


Fig. 9: Comparison of Serum insulin and HOMA with stage of hypertension

Table-11: Comparison of urea and Creatinine between with and without hypertension

	With hypertension	Without hypertension	p-value[1]
Urea	33.97±7.93	21.86±5.77	0.0001*
Creatinine	1.01±0.31	0.79±0.20	0.0001*

[1]Unpaired t-test

Table-11& Fig.10 shows the comparison of urea and Creatinine between with and without hypertension. Urea and Creatinine both were significantly (p=0.0001) higher among patients with hypertension than without hypertension.

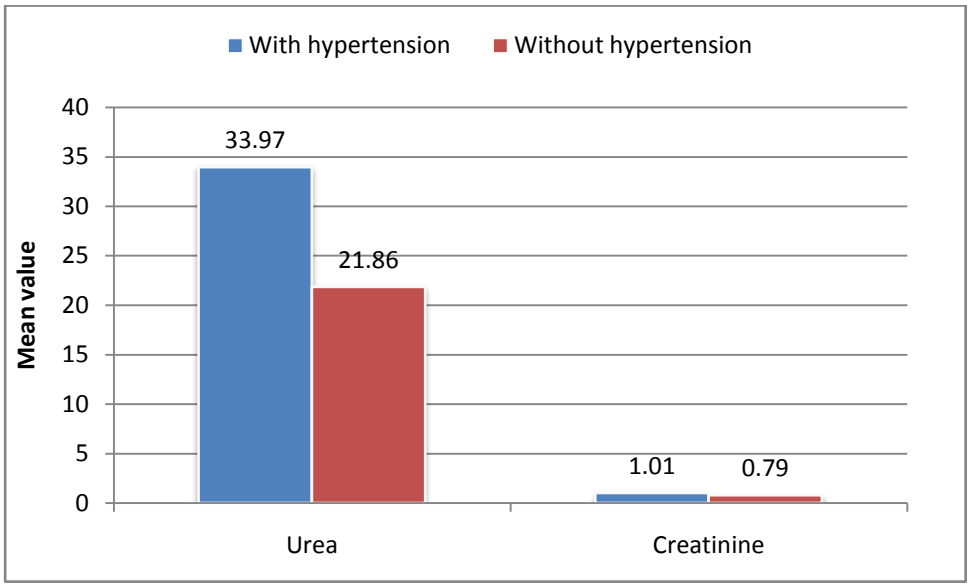


Fig. 10: Comparison of urea and Creatinine between with and without hypertension

Table-12: Comparison of ACR between with and without hypertension

	ACR **(Mean±SD)**
With hypertension	87.56±165.17
Without hypertension	27.21±31.73
p-value[1]	0.001*

[1]Mann-Whitney U test, *Significant

Table-12& Fig.11 shows the comparison of ACR between with and without hypertension. ACR significantly (p=0.001) higher among patients with hypertension (87.56±165.17) than without hypertension (27.21±31.73).

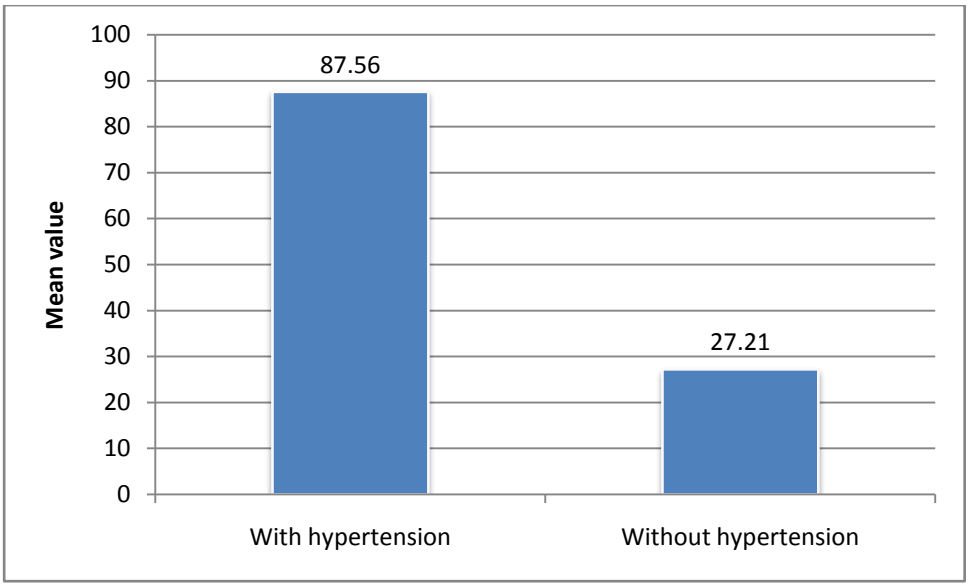


Fig. 11: Comparison of ACR between with and without hypertension

Table-13: Comparison of Lipid profile between with and without hypertension

Lipid profile	With hypertension	Without hypertension	p-value[1]
TC	201.77±54.66	192.46±33.10	0.15
TG	162.38±82.50	165.95±94.06	0.78
LDL	115.08±49.74	126.03±38.81	0.09
HDL	42.67±13.13	43.61±4.70	0.51

[1]Unpaired t-test

Table-13& Fig.12 shows the comparison of lipid profile between with and without hypertension. There was no significant (p>0.05) difference in lipid profile between with and without hypertension.

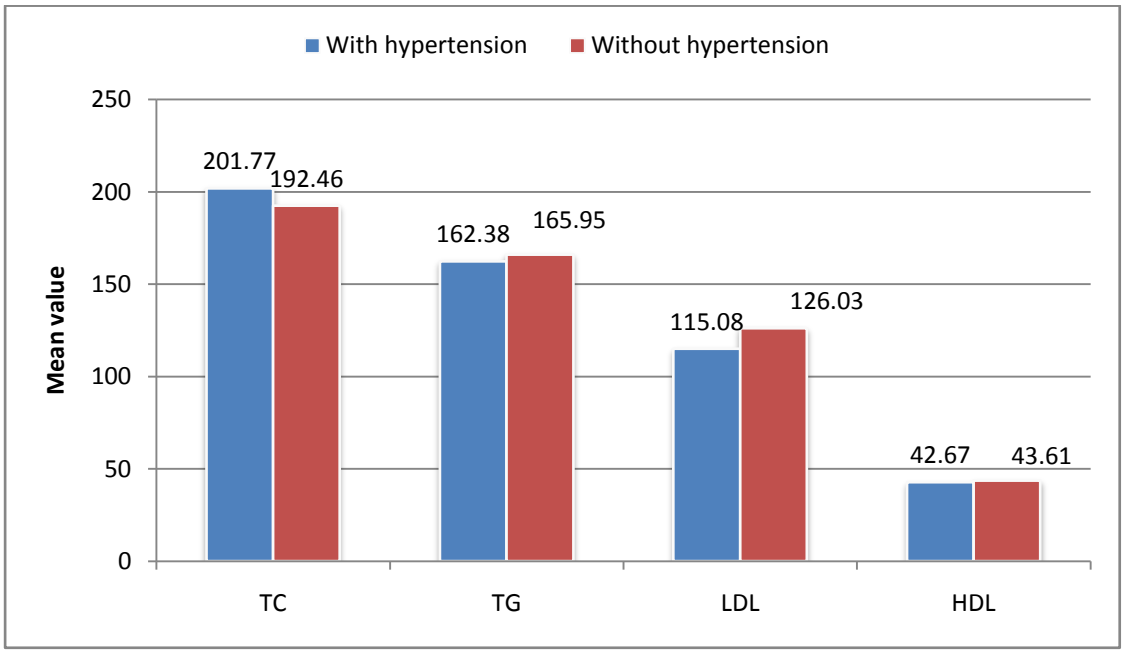


Fig. 12: Comparison of Lipid profile between with and without hypertension

Table-14: Comparison of Serum insulin and HOMA between with and without hypertension

	With hypertension	Without hypertension	p-value[1]
Serum insulin	32.61±21.16	7.98±5.38	0.0001*
HOMA	7.41±4.64	2.48±1.63	0.0001*

[1]Unpaired t-test, *Significant

Table-14 & Fig.14 shows the comparison of serum insulin and HOMA between with and without hypertension. Serum insulin and HOMA were significantly (p=0.0001) higher among patients of with hypertension than without hypertension.

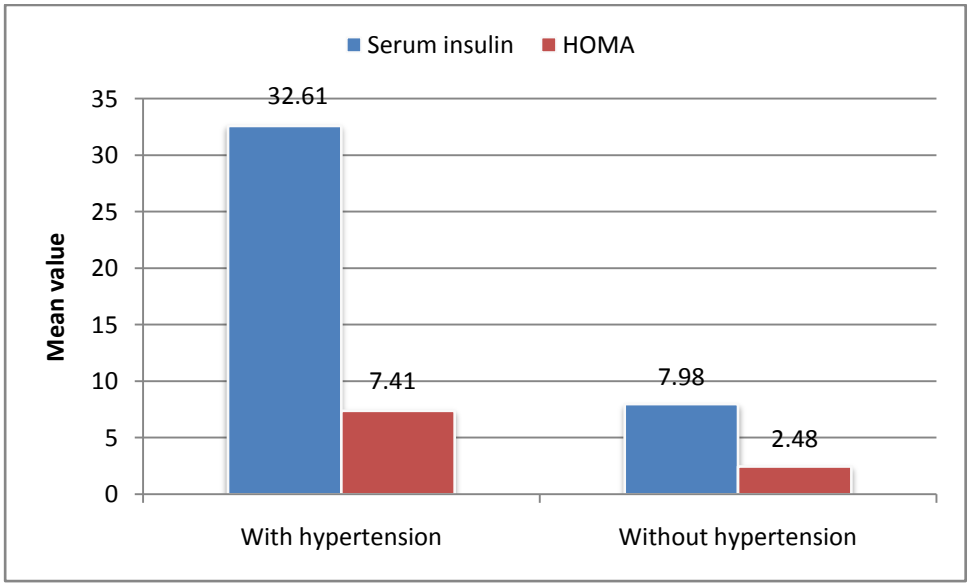


Fig. 14: Comparison of Serum insulin and HOMA between with and without hypertension

DISCUSSION

Hypertension (HTN) and cardiovascular diseases (CVDs) caused by high blood pressure blood pressure have drawn great attentions in public health (Global Burden of Disease Cancer Collaboration, 2019)[88].

More recently, the prevalence of HTN has surged, resulting in the increase of blood pressure related morbidity and death. Furthermore, the common concomitant status in prehypertensive and hypertensive individuals, such as abnormalities in glucose and lipid homeostasis, leads to a poorer long-term prognosis (Tsimihodimos et al, 2018)[89].

In fact, dyslipidemia and impaired fasting glucose (IFG) were shown to be present in 41.9 percent and 40.7 percent of hypertensive individuals, respectively (Yu et al, 2015)[90]. Aberrant glycolipid metabolism in hypertensive individuals considerably increases the risk of CVD in these patients. As a result, seeking for a better understanding of the glycolipid metabolism components in patients with HTN may help to alleviate the massive load of global disease.

Insulin resistance (IR), defined as the attenuation of insulin responsiveness in tissues, is a crucial mechanism in glycolipid metabolism. IR may be a substantially primary cause for CVD, according to current epidemiological and pathophysiology researches (Ormazabal et al, 2018)[15].

The impact of IR on the pathophysiology of HTN has also been extensively studied. Up to now, the available the reference standard for evaluating the significance of IR is the hyper insulinemiceuglycemic clamp (HEC) (Mancusi et al, 2020)[91].

However, this approach of analyzing IR, is time-consuming, costly, and sophisticated, and it necessitates a large workforce. Consequently, it is unsuitable for routine clinical use. The development of non-insulin-based IR indicators has provided an easier and less expensive method to detect IR, especially in primary healthcare settings.

The metabolic score for insulin resistance (METS-IR) index is a recently developed index aimed to be a practical and efficient alternative biomarker of IR. The METS-IR index has a stronger correlation with the HEC than other non–insulin-based IR indexes (Bello-Chavolla et al, 2018)[92].

However, there are only few studies on the association between the METS-IR index and blood pressure, with studies limited only to China and Mexico (Li et al, 2021)[93].

The present study was conducted in Department of Medicine, Santosh Medical College and hospital, Ghaziabad with the objective to study relationship of hypertension with insulin resistance. A total of 95 cases and 95 controls were included in the study.

In the present study, the mean age of patients of with and without hypertension was 53.74±8.29 and 54.07±9.03 years respectively. There was no significant ($p>0.05$) in age between with and without hypertension patients showing comparability of the groups in terms of age. There were equal no. of male and females in both the groups. Hussain and Tripathi (2017)[81] found that the mean age of the patients of hypertensive group was 49.79±17.04 years and mean age of normotensive group was 51.94±16.64 years. Male preponderance was observed in both the groups. In the study by de Morais et al (2016)[79], a total of 162 adolescents (35 with normal blood pressure and 127 with altered blood pressure) were studied; 61% (n = 99) of them were boys and the mean age was 14.9 ± 1.62 years.

In this study, the mean BMI of patients of with and without hypertension was 22.67±2.87 kg/mtr^2 and 22.98±2.66 kg/mtr^2 respectively. There was no significant ($p>0.05$) in BMI between with and without hypertension.

Stage II hypertension was among majority of patients in the current study. In the study by Quesada et al (2021)[83], Stage 1 or 2 hypertension was present in 26% of participants (mean [SD] SBP, 116.8 [15] mmHg and diastolic BP, 71.0 [10.4] mmHg).

This study found that there was no significant ($p>0.05$) difference in urea and Creatinine between stage I and stage II hypertension.

In this study, ACR was significantly ($p=0.01$) higher patients of stage II hypertension (112.73±190.71) compared to stage I (27.32±27.11).

This study revealed that there was no significant ($p>0.05$) difference in lipid profiles between with and without hypertension.

There was no significant ($p>0.05$) difference in serum insulin and HOMA between with and without hypertension in this study.

Urea and Creatinine both were significantly ($p=0.0001$) higher among patients with hypertension than without hypertension in the present study.

This study found that ACR significantly (p=0.001) higher among patients with hypertension (87.56±165.17) than without hypertension (27.21±31.73).

In the present study, there was no significant (p>0.05) difference in lipid profile between with and without hypertension. In the study by Rad et al (2020)[82], TG/HDL-C was 3.78 ± 3.28 in non-HTN and 5.76 ± 5.35 in HTN participants (p < 0.001). The frequency of all cardio-metabolic risk factors (except HDL cholesterol level) was higher in hypertensive group, after adjusting for age and gender (p < 0.001). Hussain and Tripathi (2017)[81] showed that the mean total cholesterol levels were significantly lower in hypertensive groups than that of normotensive group (p=0.03).

This study showed that Serum insulin and HOMA were significantly (p=0.0001) higher among patients of with hypertension than without hypertension. Quesada et al (2021)[83] found that there was a significant linear association between HOMA-IR and both SBP (β, 2.64±0.44) and diastolic BP (β, 1.49±0.35). Hussain and Tripathi (2017)[81] found that out of 50 from each group, 19 (38%) of hypertensive patients and 7 (14%) of normotensive patients had insulin resistance. Metabolic syndrome was noted in 23 (46%) and 10 (20%) cases of hypertensive and normotensive groups respectively and this difference was found to be statistically significant (p=0.01). The mean serum insulin levels were high in hypertensive groups than that of normotensive group which was statistically significant (p=0.00).

deMorais et al (2016)[80] reported that thirty-eight (23.5%) adolescents had altered HOMA-IR. The group with altered blood pressure had higher values of body mass index and HOMA-IR (p< 0.001), and such correlation was stronger than in the normotensive group. Logistic regression showed that HOMA-IR was as predictor of altered blood pressure (odds ratio − OR = 2.0; p = 0.001). The study concluded that there was a significant association of insulin resistance with blood pressure and the impact of insulin resistance on blood pressure since childhood. The correlation and association between markers of cardiovascular diseases was more pronounced in adolescents with altered blood pressure, suggesting that primary prevention strategies for cardiovascular risk factors should be early implemented in childhood and adolescence.

CONCLUSIONS

The present study was done in the Department of Medicine, Santosh Medical College and hospital, Ghaziabad with the objective to study the relationship of hypertension with insulin resistance. A total of 95 cases and 95 controls were included in the study. The average age of patients with and without hypertension was 53.74±8.29 and 54.07±9.03 years respectively. There was no significant ($p>0.05$) in age between with and without hypertension patients showing comparability of the groups in terms of age. The mean BMI of patients of with and without hypertension was 22.67±2.87 kg/mtr2 and 22.98±2.66 kg/mtr2 respectively. There was no significant ($p>0.05$) in BMI between with and without hypertension. Our study showed Stage II hypertension was predominant among the study population. There was no significant ($p>0.05$) difference in urea and Creatinine between stage I and stage II hypertension. ACR was significantly ($p=0.01$) higher patients of stage II hypertension (112.73±190.71) compared to stage I (27.32±27.11). There was no significant ($p>0.05$) difference in lipid profiles between with and without hypertension. Urea and Creatinine both were significantly ($p=0.0001$) higher among patients with hypertension than without hypertension. ACR significantly ($p=0.001$) higher among patients with hypertension (87.56±165.17) than without hypertension (27.21±31.73). There was no significant ($p>0.05$) difference in lipid profile between with and without hypertension. Serum insulin and HOMA were significantly ($p=0.0001$) higher among patients of with hypertension than without hypertension. Our study suggested that hypertension is notably associated with increased mean fasting insulin levels and insulin resistance and thus we conclude that hyperinsulinemia has a possible role in the pathophysiology of hypertension with insulin resistance being one of the predominant mechanisms.

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ANNEXURE

CLINICAL PROFORMA

Particulars of the patient:

1. Name:
2. Age:
3. Sex:

History:

Presenting complaints (with duration, onset, associated factors)

1. Headache
2. Dizziness
3. Nausea and Vomiting
4. Fatigue
5. Awareness of heart beat
6. History of significant cardiovascular / cerebrovascular disease / thyroid disorder.

Past History: History of Tuberculosis, Diabetes, CAD, COPD, Asthma, Seizures.

Family history: HTN, DM, TB, CAD, CVA

General Physical examination:

1. Built
2. Nutrition
3. Height(cm)/Weight(cm)/Waist(cm)
4. Waist Hip ratio:
5. BMI
6. Pallor/Icterus/Clubbing/Cyanosis/Lymphadenopathy/Edema
7. BP
8. Pulse
9. JVP

Investigations:

1. Fasting blood sugar
2. Fasting insulin
3. Plasma lipid profile
4. Renal Function Test
5. Urine Albumin Creatinine Ratio (ACR)

SANTOSH MEDICAL COLLEGE AND HOSPITAL (GHAZIABAD)

INFORMED CONSENT

I _____ Son/Daughter/Wife of _____ resident of _____.

hereby declare that I give my full, free and voluntary informed consent in the thesis **"To Study Relationship Of Hypertension With Insulin Resistance"** Dr. Naluri Mahesh has informed me to my full satisfaction, in the language I understand, about the purpose, nature of study and various laboratory investigations for the study to be carried out. I have been informed about the duration of the study and instructions to be followed during the study period.

I give full consent for being enrolled in the above study and I reserve my rights to withdraw from this study, whenever I wish without prejudice of my right to undergo further treatment at Santosh Hospital, Ghaziabad U.P.

Patient's/ Patient's relative's signature
Or thumb impression

Doctors signature

Name:

Date:

We have witnessed that the patient signed the above form in the presence of his free will after fully understanding its content.

Signature of Witness

Name

Signature of Investigator
Name: Dr. NALURI MAHESH
Designation: PG Department of General Medicine
Contact No.- 9938014106

SANTOSH MEDICAL COLLEGE & HOSPITAL

Details of Patient Information Sheet
Human Subject Research Proposal

1) Identifying Data

Name of Researcher: Dr. Naluri Mahesh

Department: Department of General medicine

Title of Project: **"To Study Relationship of Hypertension with Insulin Resistance"**

2) Description of Human Subjects Safeguards and Rights:

A) Possible psychological or physical risk or discomfort, involved in research
Yes □ NO □ (if no, skip item B)
If yes, answer the following

Why necessary?

1. To have the common disease
2. Specificity and sensitivity of the treatment

B) Make sure the following questions are answered in your research proposal on collection of Data:

1) When will it take place?
July 2021 to June 2022.

2) What length of time needed for complete examination of the patient?
Approx 1 hour.

3) What period of time needed?
Approx 1 year.

4) Which specific place within institution?
Department of medicine and pathology

5) How much population required including number of subject?
190

6) Name of instrument to be used for data collection?

1. A clinical study on risk factors, clinical presentation, Fasting blood sugar level and fasting Insulin levels will be done .Also, Plasma lipid profile, renal function test and Urine Albumin Creatinine Ratio (ACR) will be done.

7) Methodology to be used (write details)-

- All the patients will be subjected to history taking and clinical examination to diagnose primary hypertension.
- Secondary hypertension exclusion will be based on history taking , general physical examination and alcohol intake, drug intake (NSAID'S , corticosteroids, oral contraceptives),obesity, pregnancy, renal diseases (Glomerulonephritis , renal vascular disease and polycystic kidney disease),endocrine disorders (Acromegaly, hypothyroidism, thyrotoxicosis , hyperparathyroidism, Cushing syndrome, Conn syndrome, Pheochromocytoma).
- The primary hypertensive patients will be subjected to evaluation of hypertension grades as per JNC 8 Guidelines.

C) Will Subjects be given research results if they so request?
Yes □ No □

संतोष मेडिकल कॉलेज एवं अस्पताल (गाजियाबाद)

सहमति पत्र (सूचित)

मैं _____ बेटा / बेटी /पत्नी_____

निवासी _____ घोषणा करती हूं कि मैं डॉ._____, ने मुझे मेरी भाषा में अपने अध्ययन **"To Study Relationship Of Hypertension With Insulin Resistance"** अध्ययन के उद्देश्य के बारे में , और अध्ययन के दौरान अपनाई जाने वाली विभिन्न प्रयोगशाला जांच के बारे में सूचित कर दिया है। मुझे अध्ययन की अवधि और उसके दौरान अपनाए जाने वाले निर्देश भी मेरी भाषा मे समझा दिए गए है । मैं उपरोक्त अध्ययन में बिना किसी दबाव के दाखिला ले रहा हूं और पूर्ण सहमति दे रहा हूं । सन्तोष अस्पताल, गाजियाबाद में अपने आगे के उपचार पर बिना प्रतिकूल प्रभाव डाले इस अध्ययन से और प्रयोगशाला जांच की प्रकृति से मैं जब चाहूँ बाहर जाने के अपने अधिकार को सुरक्षित रख रही हूं।

रोगी / रोगी के रिश्तेदार के हस्ताक्षर डॉक्टर के हस्ताक्षर

नाम

दिनांक:

मेरी उपस्थिति में मरीज ने पूरी तरह से डॉक्टर के बताए गए अध्ययन और निर्देशों को समझने के बाद अपनी स्वतंत्र इच्छा से ऊपर के फार्म पर हस्ताक्षर किए है।

हस्ताक्षर नाम:

पदनाम: पीजी

आयुर्विज्ञान चिकित्सा विभाग

LIST OF ABBREVAITIONS

S.NO	ABBREVIATION	FULL FORM
1.	HTN	HYPERTENSION
2.	DM	DIABETES MELLITUS
3.	SNS	SYMPATHETIC NERVOUS SYSTEM
4.	RAAS	RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM
5.	CVD	CARDIOVASCULAR DISEASE
6.	ANP	ATRIAL NATRIURETIC PEPTIDE
7.	BNP	BRAIN NATRIURETIC PEPTIDE
8.	VSMC	VASCULAR SMOOTH MUSCLE CELL
9.	MAPK	MITOGEN-ACTIVATED PROTEIN KINASE
10.	HOMA-IR	HOMEOSTASIS MODEL ASSESSMENT OF INSULIN RESISTANCE
11.	METS-IR	METABOLIC SCORE FOR IR

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F. No. SU/2021/1830[16] Dated: 17.07.2021

Subject: Grant of Ethical Clearance for Thesis Protocol Topic "**TO STUDY RELATIONSHIP OF HYPERTENSION WITH INSULIN RESISTANCE",** submitted by **Dr. Naluri Mahesh,** MD/MS student of Batch 2020-2021, Department of **General Medicine**.

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"TO STUDY RELATIONSHIP OF HYPERTENSION WITH INSULIN RESISTANCE", Dr. Naluri Mahesh** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 19.03.2021, 22.03.2021, 24.03.2021, 25.03.2021, 26.03.2021, 27.03.2021 and 06.04.2021. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **12.07.2021** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. V. P. Gupta]
REGISTRAR

SANTOSH "DEEMED TO BE UNIVERSITY" REGISTRAR GHAZIABAD, NCR DELHI

Dr. Naluri Mahesh
MD/MS student of batch 2020-2021
Department of General Medicine
Email: maheshn.nmahesh@gmail.com

Copy to:

1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Research
4. The Dean – Academics
5. The Director - IQAC
6. Dr. Ashok Kumar (Guide)
7. HOD of **General Medicine**

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MASTER CHART

SR. NO.	AGE	SEX	BMI	SBP (mm of Hg)	DBP (mm of Hg)	B. UREA (mg/dl)	S. CREATININE (mg/dl)	ACR	TC	TG	LDL	HDL	FBS	S.INSULIN	HOMA
1	54	M	18	108	80	10	0.6	23	180	316	98	41	150	7.7	3.03
2	61	M	19	120	70	12	0.9	12	234	151	170	38	90	6	1.33
3	62	M	19	124	64	16	0.3	25	243	37	146	32	120	8.1	2.39
4	61	M	20	98	70	18	1.1	11	190	224	126	42	290	1.35	0.96
5	50	F	22	120	70	26	1	16	236	184	192	41	100	4.4	1.08
6	51	F	24	90	76	28	0.6	18	162	94	110	43	180	2.7	1.19
7	50	F	24	96	76	22	0.6	26	208	88	116	45	110	6.9	1.87
8	61	F	20	100	78	20	0.8	28	190	228	136	38	123	3.8	1.15
9	67	F	20	116	88	22	0.9	17	161	114	98	51	117	13.3	3.83
10	72	M	20	122	84	21	0.6	19	184	190	96	45	140	7	2.41
11	42	M	23	120	82	16	0.6	15	148	58	68	46	130	23	7.05
12	43	M	24	120	82	18	1.1	26	154	68	152	48	120	18	5.32
13	48	F	19	108	80	24	0.6	22	203	109	65	44	180	9	3.99
14	51	M	20	120	70	22	0.6	21	174	104	102	52	110	12	3.25
15	60	F	20	124	64	24	1.1	23	178	176	110	40	145	11	3.93
16	59	F	20	98	70	28	0.9	12	156	180	127	44	119	7.7	2.26
17	56	M	23.5	120	70	16	0.6	25	216	96	130	43	139	6	2.05
18	60	M	22	90	76	16	1	11	170	84	98	52	142	8	2.83
19	59	M	20	96	76	30	0.6	16	197	352	156	40	120	1.35	0.39
20	44	F	23	100	78	34	0.9	18	164	170	110	46	118	4.4	1.28
21	59	M	19	116	88	26	0.6	26	197	276	138	44	110	2.7	0.73
22	60	F	18	122	84	22	0.6	28	164	96	65	46	119	6.9	2.02
23	48	F	20	120	82	16	0.6	17	177	95	114	50	98	3.8	0.91
24	48	F	21	120	82	18	1.1	19	267	218	226	40	240	3.3	1.95
25	51	M	21	116	88	18	1	15	250	357	176	39	110	7	1.89
26	46	F	21	122	84	16	0.6	26	170	105	109	41	142	23	7.7
27	51	M	23	120	82	14	0.6	22	163	57	95	41	92	18	4.08
28	51	F	21	120	82	24	0.8	21	244	386	168	37	133	9	2.9
29	43	M	21	108	80	28	0.9	12	248	292	196	39	99	12	2.93
30	44	F	20	120	70	22	0.6	25	243	37	146	32	120	8.1	2.39
31	46	F	20	124	64	18	0.6	11	190	224	126	42	290	1.35	0.96
32	51	F	23	98	70	16	1.1	16	236	184	192	41	100	4.4	1.08
33	45	F	19	120	70	28	0.6	18	162	94	110	43	180	2.7	1.19
34	50	F	24	90	76	30	0.6	26	208	88	116	45	110	6.9	1.87
35	52	M	24	108	80	34	1.1	28	190	228	136	38	123	3.8	1.15
36	45	F	23	120	70	32	0.9	17	161	114	98	51	117	13.3	3.83
37	44	M	26	124	64	20	0.6	19	184	190	96	45	140	7	2.41
38	58	F	23.5	98	70	22	1	15	148	58	68	46	130	23	7.05
39	45	F	28	120	70	28	0.6	26	154	68	152	48	120	18	5.32
40	64	M	24	90	76	24	0.9	22	203	109	65	44	180	9	3.99
41	68	F	24	96	76	28	0.6	21	174	104	102	52	110	12	3.25
42	42	F	26	100	78	21	0.6	23	178	176	110	40	145	11	3.93
43	61	M	23.5	116	88	14	0.6	12	156	180	127	44	119	7.7	2.26
44	46	F	26	122	84	15	1.1	130	216	96	130	43	139	6	2.05
45	58	F	20	120	82	16	1	11	170	84	98	52	142	8	2.83
46	49	F	27	120	82	18	0.6	16	197	352	156	40	120	1.35	0.39
47	57	F	20	108	80	20	0.6	18	164	170	110	46	118	4.4	1.28
48	47	M	28	120	70	22	0.8	26	197	276	138	44	110	2.7	0.73
49	63	F	22	124	64	25	0.9	28	164	96	65	46	119	6.9	2.02
50	47	M	28	98	70	26	0.6	17	177	95	114	50	98	3.8	0.91
51	47	F	27	120	70	20	1.1	19	267	218	226	40	240	3.3	1.95
52	57	M	23.5	90	76	22	0.6	15	250	357	176	39	110	7	1.89
53	45	F	24	96	76	28	0.6	26	174	104	102	52	110	12	3.25
54	61	F	22	100	78	29	1.1	22	178	176	110	40	145	11	3.93
55	49	M	25	116	88	18	0.9	21	156	180	127	44	119	7.7	2.26
56	48	F	25	122	84	18	0.6	12	216	96	130	43	139	6	2.05
57	58	M	20	120	82	20	1	25	170	84	98	52	142	8	2.83
58	57	M	26.5	120	82	26	0.6	11	197	352	156	40	120	1.35	0.39
59	61	M	20	116	88	25	1.1	16	164	170	110	46	118	4.4	1.28
60	61	F	26	122	84	28	1	18	197	276	138	44	110	2.7	0.73
61	44	F	24	120	82	16	0.6	210	164	96	65	46	119	6.9	2.02
62	61	F	22	120	82	18	0.6	28	177	95	114	50	98	3.8	0.91
63	63	F	21	108	80	12	0.8	17	267	218	226	40	240	3.3	1.95
64	71	M	28	120	70	17	0.9	19	250	357	176	39	110	7	1.89
65	78	F	25	124	64	22	0.6	80	170	105	109	41	142	23	7.7
66	57	F	22	98	70	26	0.6	26	163	57	95	41	92	18	4.08
67	45	F	25	120	70	33	1.1	22	244	386	168	37	133	9	2.9
68	43	F	26	90	76	32	0.6	21	248	292	196	39	99	12	2.93
69	52	M	23	98	70	25	0.7	200	243	37	146	32	120	8.1	2.39
70	50	F	29	120	70	18	1.1	12	190	224	126	42	290	1.35	0.96
71	44	M	28	90	76	14	0.9	25	236	184	192	41	100	4.4	1.08
72	57	F	22	96	76	12	0.7	110	162	94	110	43	180	2.7	1.19
73	44	M	26	100	78	10	1	16	208	88	116	45	110	6.9	1.87
74	45	F	22	116	88	24	0.6	18	190	228	136	38	123	3.8	1.15
75	46	F	30	122	84	32	0.9	26	161	114	98	51	117	13.3	3.83
76	42	M	27	124	80	30	0.7	28	184	190	96	45	140	7	2.41
77	52	M	23	98	70	32	0.7	17	148	58	68	46	130	23	7.05
78	57	F	26	120	64	22	1.1	90	154	68	152	48	120	18	5.32
79	57	M	26	90	70	24	1	15	203	109	65	44	180	9	3.99
80	49	M	24	96	70	26	0.7	26	174	104	102	52	110	12	3.25
81	54	F	20	100	76	28	0.7	22	178	176	110	40	145	11	3.93
82	56	F	20	116	70	28	0.8	21	156	180	127	44	119	7.7	2.26
83	51	M	20	122	70	16	0.9	12	216	96	130	43	139	6	2.05
84	46	M	23	120	76	18	0.7	25	170	84	98	52	142	8	2.83
85	43	M	24	120	76	14	0.7	11	197	352	156	40	120	1.35	0.39
86	49	F	19	108	78	18	1.1	16	164	170	110	46	118	4.4	1.28
87	79	M	20	120	88	16	0.7	18	197	276	138	44	110	2.7	0.73
88	81	F	20	124	84	18	0.7	26	164	96	65	46	119	6.9	2.02
89	73	F	20	98	76	20	1.1	28	177	95	114	50	98	3.8	0.91
90	56	M	23.5	120	78	22	0.9	17	267	218	226	40	240	3.3	1.95
91	60	M	22	90	88	24	0.7	19	250	357	176	39	110	7	1.89
92	70	M	20	96	84	26	1	15	208	88	116	45	110	6.9	1.87
93	44	F	23	100	82	20	0.8	26	190	228	136	38	123	3.8	1.15
94	60	M	19	116	82	22	0.8	22	161	114	98	51	117	13.3	3.83
95	64	F	18	122	80	24	1.1	21	184	190	96	45	140	7	2.41

SR. NO.	AGE	SEX	BMI	SBP (mm of Hg)	DBP (mm of Hg)	stage of hypertension	B. UREA (mg/dl)	ATININE	ACR	TC	TG	LDL	HDL	FBS	S.INSULIN	HOMA
1	52	M	19	140	90	STAGE 1	34	0.9	16	180	316	98	40	89	32	7.02
2	62	M	19	130	90	STAGE 1	45	1.2	18	234	307	146	32	108	33	9.6
3	44	F	20	136	94	STAGE 1	60	1	26	190	214	43	30	90	32	7.1
4	52	F	20	134	98	STAGE 1	36	0.8	11	208	88	116	45	118	38	11.06
5	52	M	20	138	94	STAGE 1	36	0.9	28	154	68	93	48	83	28	5.73
6	58	F	18	130	90	STAGE 1	34	1.2	15	256	112	196	41	90	42	9.32
7	51	M	23	132	94	STAGE 1	37	1.1	110	278	70	156	45	92	38	8.6
8	43	M	21	156	86	STAGE 1	39	0.6	16	302	209	251	40	115	42	11.9
9	54	M	26	130	90	STAGE 1	36	0.6	22	248	292	112	39	85	52	10.9
10	54	F	23.5	132	94	STAGE 1	43	0.9	21	164	128	99	49	89	7	1.5
11	46	F	24	148	90	STAGE 1	29	0.8	130	267	218	154	40	107	33	8.7
12	46	F	20	130	92	STAGE 1	30	1.9	26	250	357	176	39	80	32	6.3
13	49	F	27	130	90	STAGE 1	25	1.1	28	210	136	30	40	90	15	3.3
14	61	F	22	136	92	STAGE 1	33	0.7	15	176	172	154	50	100	41	10.1
15	47	M	28	140	96	STAGE 1	28	1.1	40	210	106	112	38	103	4	1.01
16	49	F	22	138	94	STAGE 1	33	1	25	243	307	146	32	83	84	17.19
17	49	M	25	156	90	STAGE 1	27	0.9	11	159	148	100	32	79	90	17.5
18	48	F	25	154	90	STAGE 1	34	0.9	16	163	160	32	28	92	31	7.03
19	44	F	24	158	90	STAGE 1	33	1.16	19	276	292	167	32	93	84	19.2
20	81	M	28	150	90	STAGE 1	37	1.5	22	244	386	171	37	70	60	10.3
21	45	F	25	152	96	STAGE 1	37	0.6	12	291	161	48	38	96	20	4.7
22	43	F	26	144	90	STAGE 1	43	0.7	25	81	96	112	46	110	9	2.4
23	50	F	29	154	90	STAGE 1	29	0.9	16	143	92	163	41	83	29	5.9
24	44	M	28	168	100	STAGE 1	33	0.9	18	196	112	32	42	82	5	1.01
25	54	F	20	136	94	STAGE 1	60	1	11	278	70	156	45	92	38	8.6
26	47	F	20	134	98	STAGE 1	36	0.8	19	154	68	93	48	83	28	5.73
27	44	M	20	138	94	STAGE 1	36	0.9	21	269	137	40	45	113	36	10.1
28	61	F	18	130	90	STAGE 1	34	1.2	28	170	186	128	54	86	8	1.67
29	52	M	18	140	100	STAGE 2	23	1.1	70	115	109	66	27	81	72	14.3
30	61	M	20	150	100	STAGE 2	50	0.5	26	185	88	116	51	113	37	10.31
31	50	F	22	166	100	STAGE 2	45	1.3	330	207	134	138	42	77	472	89.6
32	51	F	24	158	90	STAGE 2	36	0.6	380	243	307	146	32	83	84	17.19
33	50	F	24	146	102	STAGE 2	28	0.7	130	159	148	100	32	79	90	17.5
34	44	F	20	150	90	STAGE 2	40	0.9	15	163	160	32	28	92	31	7.03
35	44	M	20	162	110	STAGE 2	28	1.4	22	139	59	73	54	113	54	15.05
36	67	M	23	170	100	STAGE 2	39	1.18	80	159	140	78	33	117	46	13.2
37	43	M	24	158	106	STAGE 2	26	1.09	23	243	132	139	38	97	58	13.8
38	52	F	19	164	90	STAGE 2	40	0.9	800	190	224	126	42	88	2.9	0.62
39	65	M	20	170	90	STAGE 2	33	0.8	110	236	184	192	40	89	32	7.02
40	72	F	20	178	100	STAGE 2	28	0.7	16	190	214	118	30	81	33	6.59
41	56	M	23.5	162	110	STAGE 2	29	0.9	18	268	185	42	38	113	36	10.03
42	60	M	22	146	100	STAGE 2	42	0.7	26	148	58	90	46	77	32	6.07
43	44	F	23	162	100	STAGE 2	38	1.1	980	235	146	156	42	79	53	10.3
44	55	M	19	170	110	STAGE 2	29	0.7	660	177	76	124	38	92	16	3.4
45	55	F	20	150	100	STAGE 2	42	1.1	26	269	137	40	45	113	36	10.1
46	48	F	21	154	96	STAGE 2	45	0.8	210	186	164	116	40	81	17	3.39
47	51	M	21	160	100	STAGE 2	56	0.9	40	239	97	172	42	118	32	9.31
48	46	F	21	176	90	STAGE 2	20	0.7	80	170	186	128	54	86	8	1.67
49	51	F	21	144	100	STAGE 2	28	1	11	186	88	116	45	110	12	3.2
50	44	F	20	148	100	STAGE 2	45	1.4	18	101	172	88	106	99	9	2.1
51	46	F	20	156	110	STAGE 2	25	0.9	26	180	316	29	40	80	38	7.49
52	54	F	23	164	96	STAGE 2	34	0.7	40	247	212	147	25	92	6	1.36
53	55	F	19	180	100	STAGE 2	37	0.9	17	276	292	167	32	93	84	19.2
54	50	F	24	176	110	STAGE 2	28	1.9	450	237	156	89	42	113	52	13.2
55	52	M	24	152	104	STAGE 2	42	0.7	15	72	98	128	42	100	8	1.9
56	55	F	23	160	100	STAGE 2	27	1.1	26	244	386	171	37	70	60	10.3
57	45	F	28	158	102	STAGE 2	20	1	90	291	161	48	38	96	20	4.7
58	55	M	24	168	100	STAGE 2	31	1.1	110	81	96	112	46	110	9	2.4
59	42	F	26	178	110	STAGE 2	32	0.8	60	143	92	163	41	83	29	5.9
60	46	M	23.5	174	100	STAGE 2	28	0.6	600	196	112	32	42	82	5	1.01
61	46	F	26	182	112	STAGE 2	26	1	210	196	82	125	46	89	11	2.41
62	46	F	20	166	100	STAGE 2	42	0.9	17	267	218	96	40	97	28	6.69
63	47	M	28	164	100	STAGE 2	35	0.8	19	164	90	39	42	99	2	0.48
64	47	F	27	160	100	STAGE 2	25	1.9	280	234	307	146	32	108	33	9.6
65	57	M	23.5	160	100	STAGE 2	31	1.2	60	185	88	116	51	113	37	10.31
66	45	F	24	168	110	STAGE 2	44	1	90	207	134	138	42	77	472	89.6
67	58	M	20	160	90	STAGE 2	27	0.7	120	190	214	43	30	90	32	7.1
68	57	M	26.5	168	100	STAGE 2	28	1	210	101	172	88	106	99	9	2.1
69	48	M	20	166	106	STAGE 2	24	1.5	28	180	316	29	40	80	38	7.49
70	61	F	26	162	104	STAGE 2	25	1.8	17	247	212	147	25	92	6	1.36
71	61	F	22	156	100	STAGE 2	31	1	80	237	156	89	42	113	52	13.2
72	48	F	21	166	108	STAGE 2	34	1.4	26	72	98	128	42	100	8	1.9
73	45	F	25	170	110	STAGE 2	26	1.5	21	248	292	112	39	85	52	10.9
74	45	F	22	168	100	STAGE 2	28	1.8	200	164	128	99	49	89	7	1.5
75	52	M	23	162	96	STAGE 2	44	0.9	110	267	218	154	40	107	33	8.7
76	45	F	22	160	104	STAGE 2	28	1	26	196	82	125	46	89	11	2.41
77	44	M	26	160	100	STAGE 2	22	1.1	28	148	58	90	46	77	32	6.07
78	45	F	22	160	100	STAGE 2	41	1.8	17	154	68	93	48	83	28	5.73
79	46	F	30	162	94	STAGE 2	40	0.8	90	235	146	156	42	79	53	10.3
80	42	M	27	164	110	STAGE 2	29	0.9	15	177	76	124	38	92	16	3.4
81	52	M	23	176	100	STAGE 2	28	1.7	26	256	112	196	41	90	42	9.32
82	45	F	26	170	110	STAGE 2	30	0.8	22	269	137	40	45	113	36	10.1
83	48	M	26	168	100	STAGE 2	27	0.9	21	186	164	116	40	81	17	3.39
84	61	M	24	162	96	STAGE 2	29	1.1	12	239	97	172	42	118	32	9.31
85	50	F	20	150	90	STAGE 2	40	0.9	25	170	186	128	54	86	8	1.67
86	56	M	20	162	110	STAGE 2	28	1.4	16	186	88	116	45	110	12	3.2
87	59	M	23	170	100	STAGE 2	39	1.18	18	302	209	251	40	115	42	11.9
88	43	M	24	158	106	STAGE 2	26	1.09	26	101	172	88	106	99	9	2.1
89	48	F	19	164	90	STAGE 2	40	0.9	28	180	316	29	40	80	38	7.49
90	60	M	20	170	90	STAGE 2	33	0.8	17	148	58	90	46	77	32	6.07
91	63	F	20	178	100	STAGE 2	28	0.7	15	235	146	156	42	79	53	10.3
92	56	M	23.5	162	110	STAGE 2	29	0.9	26	177	76	124	38	92	16	3.4
93	60	M	22	146	100	STAGE 2	42	0.7	22	256	112	196	41	90	42	9.32
94	44	F	23	162	100	STAGE 2	38	1.1	60	186	164	116	40	81	17	3.39
95	41	M	19	170	110	STAGE 2	29	0.7	50	239	97	172	42	118	32	9.31